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(71) Applicant (for all designated States except US): CORIXA CORPORATION [US/US]; 1124 Columbia Street, Suite 200, Seattle, WA 98104 (US).

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(72) Inventors; and

(75) **Inventors/Applicants (for US only):** **LODES, Michael, J.** [US/US]; 9223 36th Avenue S.W., Seattle, WA 98126 (US). **WANG, Tongtong** [US/US]; 8049 N.E. 28th Street, Medina, WA 98039 (US). **MOHAMATH, Raodoh** [US/US]; 4205 South Morgan, Seattle, WA 98118 (US). **INDIRIAS, Carol, Yoseph** [US/US]; 1541 N.W. 52nd Street, Seattle, WA 98107 (US).

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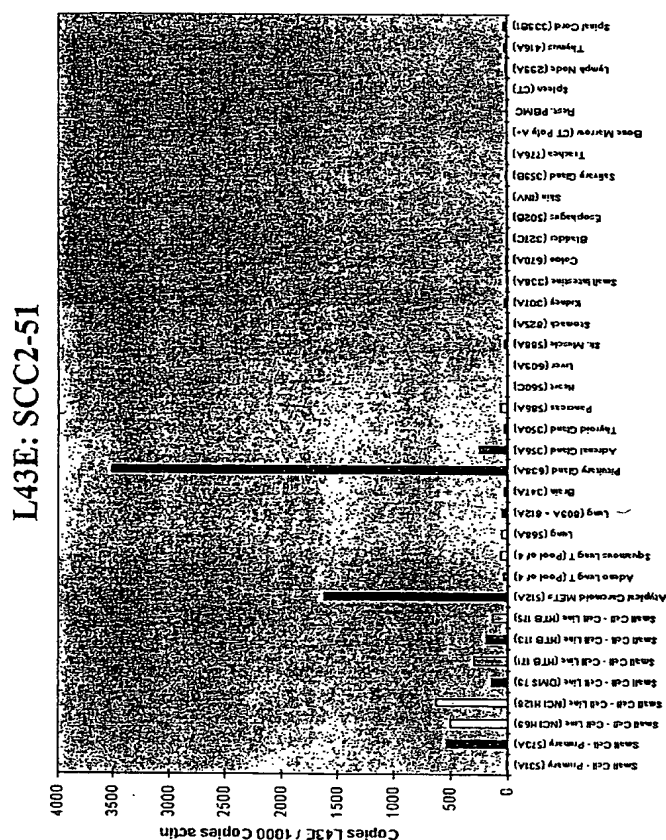
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(74) Agents: VERNIA, James, M. et al.; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).

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(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF LUNG CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly lung cancer, are disclosed. Illustrative compositions comprise one or more lung tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly lung cancer.



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COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF LUNG CANCER

TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of
5 cancer, such as lung cancer. the invention is more specifically related to polypeptides,
comprising at least a portion of a lung tumor protein, and to polynucleotides encoding
such polypeptides. such polypeptides and polynucleotides are useful in pharmaceutical
compositions, *e.g.*, vaccines, and other compositions for the diagnosis and treatment of
lung cancer.

10 BACKGROUND OF THE INVENTION

Lung cancer is the primary cause of cancer death among both men and
women in the U.S., with an estimated 172,000 new cases being reported in 1994. The
five-year survival rate among all lung cancer patients, regardless of the stage of disease
at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among
15 cases detected while the disease is still localized. However, only 16% of lung cancers
are discovered before the disease has spread.

Early detection is difficult since clinical symptoms are often not seen
until the disease has reached an advanced stage. Currently, diagnosis is aided by the use
of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic
20 examination of the bronchial passages. Treatment regimens are determined by the type
and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In
spite of considerable research into therapies for the disease, lung cancer remains
difficult to treat.

Accordingly, there remains a need in the art for improved vaccines,
25 treatment methods and diagnostic techniques for lung cancer.

SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide
compositions comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440;

(b) complements of the sequences provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440;

5 (c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440;

(d) sequences that hybridize to a sequence provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440, under moderately stringent conditions;

10 (e) sequences having at least 75% identity to a sequence of SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440; and

(g) degenerate variants of a sequence provided in SEQ ID NO:1-232,
15 243-396, 398-412, 414-424 and 437-440.

In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of lung tumor samples tested, at a level that is
20 at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for normal tissues.

The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above. In certain specific embodiments, the present invention
25 provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO:229-232, 237-242, 397, 413 and 425-436.

In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of
30 eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID
5 NOs: 229-232, 237-242, 397, 413 and 425-436, or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NOs: 1-232, 243-396, 398-412, 414-424 and 437-440.

The present invention further provides polynucleotides that encode a
10 polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

15 Within a related aspect of the present invention, the pharmaceutical compositions, *e.g.*, vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or polynucleotide of the invention and an immunostimulant, such as an adjuvant.

The present invention further provides pharmaceutical compositions that
20 comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as
25 described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, pharmaceutical compositions are provided that
30 comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides

encoding such fusion proteins, typically in the form of pharmaceutical compositions, *e.g.*, vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic polypeptides or portions/variants thereof, as described herein, and may further comprise
5 one or more polypeptide segments for facilitating the expression, purification and/or immunogenicity of the polypeptide(s).

Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient, comprising administering a pharmaceutical composition described herein. The
10 patient may be afflicted with lung cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a
15 patient a pharmaceutical composition as recited above. The patient may be afflicted with lung cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological
20 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological
25 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that
30 expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer, preferably a lung cancer, in a patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that

hybridizes to a polynucleotide that encodes a polypeptide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a polypeptide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 is a bar graph showing expression of clone SCC2-51 in normal tissues and tumor tissues.

SEQ ID NO:1 is the determined cDNA sequence for LSC-1.
SEQ ID NO:2 is the determined cDNA sequence for LSC-2.
SEQ ID NO:3 is the determined cDNA sequence for LSC-3.
SEQ ID NO:4 is the determined cDNA sequence for LSC-5.
5 SEQ ID NO:5 is the determined cDNA sequence for LSC-6.
SEQ ID NO:6 is the determined cDNA sequence for LSC-7.
SEQ ID NO:7 is the determined cDNA sequence for LSC-9.
SEQ ID NO:8 is the determined cDNA sequence for LSC-10.
SEQ ID NO:9 is the determined cDNA sequence for LSC-11.
10 SEQ ID NO:10 is the determined cDNA sequence for LSC-13.
SEQ ID NO:11 is the determined cDNA sequence for LSC-15.
SEQ ID NO:12 is the determined cDNA sequence for LSC-20.
SEQ ID NO:13 is the determined cDNA sequence for LSC-23.
SEQ ID NO:14 is the determined cDNA sequence for LSC-24.
15 SEQ ID NO:15 is the determined cDNA sequence for LSC-25.
SEQ ID NO:16 is the determined cDNA sequence for LSC-26.
SEQ ID NO:17 is the determined cDNA sequence for LSC-27.
SEQ ID NO:18 is the determined cDNA sequence for LSC-28.
SEQ ID NO:19 is the determined cDNA sequence for LSC-29.
20 SEQ ID NO:20 is the determined cDNA sequence for LSC-30.
SEQ ID NO:21 is the determined cDNA sequence for LSC-31.
SEQ ID NO:22 is the determined cDNA sequence for LSC-33.
SEQ ID NO:23 is the determined cDNA sequence for LSC-34.
SEQ ID NO:24 is the determined cDNA sequence for LSC-35.
25 SEQ ID NO:25 is the determined cDNA sequence for LSC-37.
SEQ ID NO:26 is the determined cDNA sequence for LSC-39.
SEQ ID NO:27 is the determined cDNA sequence for LSC-43.
SEQ ID NO:28 is the determined cDNA sequence for LSC-46.
SEQ ID NO:29 is the determined cDNA sequence for LSC-49.
30 SEQ ID NO:30 is the determined cDNA sequence for LSC-51.
SEQ ID NO:31 is the determined cDNA sequence for LSC-53.
SEQ ID NO:32 is the determined cDNA sequence for LSC-55.

SEQ ID NO:33 is the determined cDNA sequence for LSC-60.
SEQ ID NO:34 is the determined cDNA sequence for LSC-62.
SEQ ID NO:35 is the determined cDNA sequence for LSC-64.
SEQ ID NO:36 is the determined cDNA sequence for LSC-65.
5 SEQ ID NO:37 is the determined cDNA sequence for LSC-71.
SEQ ID NO:38 is the determined cDNA sequence for LSC-72.
SEQ ID NO:39 is the determined cDNA sequence for LSC-74.
SEQ ID NO:40 is the determined cDNA sequence for LSC-76.
SEQ ID NO:41 is the determined cDNA sequence for LSC-77.
10 SEQ ID NO:42 is the determined cDNA sequence for LSC-78.
SEQ ID NO:43 is the determined cDNA sequence for LSC-81.
SEQ ID NO:44 is the determined cDNA sequence for LSC-93.
SEQ ID NO:45 is the determined cDNA sequence for LSC-101.
SEQ ID NO:46 is the determined cDNA sequence for LSC-102.
15 SEQ ID NO:47 is the determined cDNA sequence for LSC-103.
SEQ ID NO:48 is the determined cDNA sequence for LSC-105.
SEQ ID NO:49 is the determined cDNA sequence for LSC-110.
SEQ ID NO:50 is the determined cDNA sequence for LSC-125.
SEQ ID NO:51 is the determined cDNA sequence for LSC-134.
20 SEQ ID NO:52 is the determined cDNA sequence for LSC-142.
SEQ ID NO:53 is the determined cDNA sequence for LSC-144.
SEQ ID NO:54 is the determined cDNA sequence for LSC-148.
SEQ ID NO:55 is the determined cDNA sequence for LSC-149.
SEQ ID NO:56 is the determined cDNA sequence for LSC-153.
25 SEQ ID NO:57 is the determined cDNA sequence for LSC-163.
SEQ ID NO:58 is the determined cDNA sequence for LSC-170.
SEQ ID NO:59 is the determined cDNA sequence for LSC-171.
SEQ ID NO:60 is the determined cDNA sequence for LSC-172.
SEQ ID NO:61 is the determined cDNA sequence for LSC-175.
30 SEQ ID NO:62 is the determined cDNA sequence for LSC-177.
SEQ ID NO:63 is the determined cDNA sequence for LSC-182.
SEQ ID NO:64 is the determined cDNA sequence for LSC-184.

SEQ ID NO:65 is the determined cDNA sequence for LSC-189.
SEQ ID NO:66 is the determined cDNA sequence for LSC-194.
SEQ ID NO:67 is the determined cDNA sequence for LSC-195.
SEQ ID NO:68 is the determined cDNA sequence for LSC-196.
5 SEQ ID NO:69 is the determined cDNA sequence for LSC-199.
SEQ ID NO:70 is the determined cDNA sequence for LSC-202.
SEQ ID NO:71 is the determined cDNA sequence for LSC-203.
SEQ ID NO:72 is the determined cDNA sequence for LSC-205.
SEQ ID NO:73 is the determined cDNA sequence for LSC-206.
10 SEQ ID NO:74 is the determined cDNA sequence for LSC-210.
SEQ ID NO:75 is the determined cDNA sequence for LSC-215.
SEQ ID NO:76 is the determined cDNA sequence for LSC-218.
SEQ ID NO:77 is the determined cDNA sequence for clone 48060.
SEQ ID NO:78 is the determined cDNA sequence for clone 48069.
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SEQ ID NO:80 is the determined cDNA sequence for clone 48080.
SEQ ID NO:81 is the determined cDNA sequence for clone 48090.
SEQ ID NO:82 is the determined cDNA sequence for clone 48102.
SEQ ID NO:83 is the determined cDNA sequence for clone 48112.
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SEQ ID NO:85 is the determined cDNA sequence for clone 48125.
SEQ ID NO:86 is the determined cDNA sequence for clone 48129.
SEQ ID NO:87 is the determined cDNA sequence for clone 48134.
SEQ ID NO:88 is the determined cDNA sequence for clone 48135.
25 SEQ ID NO:89 is the determined cDNA sequence for clone 48137.
SEQ ID NO:90 is the determined cDNA sequence for clone 48138.
SEQ ID NO:91 is the determined cDNA sequence for clone 48142.
SEQ ID NO:92 is the determined cDNA sequence for clone 48143.
SEQ ID NO:93 is the determined cDNA sequence for clone 48149.
30 SEQ ID NO:94 is the determined cDNA sequence for clone 48150.
SEQ ID NO:95 is the determined cDNA sequence for clone 48179.
SEQ ID NO:96 is the determined cDNA sequence for clone 48183.

SEQ ID NO:97 is the determined cDNA sequence for clone 48193.

SEQ ID NO:98 is the determined cDNA sequence for clone 48196.

SEQ ID NO:99 is the determined cDNA sequence for clone 48202.

SEQ ID NO:100 is the determined cDNA sequence for clone 48204.

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SEQ ID NO:102 is the determined cDNA sequence for clone 48206.

SEQ ID NO:103 is the determined cDNA sequence for clone 48211.

SEQ ID NO:104 is the determined cDNA sequence for clone 48216.

SEQ ID NO:105 is the determined cDNA sequence for clone 48219.

10 SEQ ID NO:106 is the determined cDNA sequence for clone 48223.

SEQ ID NO:107 is the determined cDNA sequence for clone 48224.

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SEQ ID NO:109 is the determined cDNA sequence for clone 48228.

SEQ ID NO:110 is the determined cDNA sequence for clone 48236.

15 SEQ ID NO:111 is the determined cDNA sequence for clone lcl/15745.

SEQ ID NO:112 is the determined cDNA sequence for clone lcl/16256.

SEQ ID NO:113 is the determined cDNA sequence for clone lcl/21736.

SEQ ID NO:114 is the determined cDNA sequence for clone lcl/22291.

SEQ ID NO:115 is the determined cDNA sequence for clone lcl/24845.

20 SEQ ID NO:116 is the determined cDNA sequence for clone lcl/24847.

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SEQ ID NO:119 is the determined cDNA sequence for clone lcl/24851.

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30 SEQ ID NO:222 is the determined cDNA sequence for clone SCC2-232.
SEQ ID NO:223 is the determined cDNA sequence for clone SCC2-236.
SEQ ID NO:224 is the determined cDNA sequence for clone SCC2-260.

SEQ ID NO:225 is the determined cDNA sequence for clone SCC2-261.

SEQ ID NO:226 is the determined cDNA sequence for clone SCC2-266.

SEQ ID NO:227 is the determined cDNA sequence for clone SCC2-275.

SEQ ID NO:228 is the determined cDNA sequence for clone SCC2-283.

5 SEQ ID NO:229 is the determined cDNA extended sequence for clone
SCC2-5, which relates to SEQ ID NO:146.

SEQ ID NO:230 is the determined cDNA extended sequence for clone
SCC2-14, which relates to SEQ ID NO:153.

SEQ ID NO:231 is the determined cDNA sequence for clone SCC2-50.

10 SEQ ID NO:232 is the determined cDNA extended sequence for clone
SCC2-51, which relates to SEQ ID NO:175.

SEQ ID NO:233 is the amino acid sequence encoded by SEQ ID
NO:229.

15 SEQ ID NO:234 is the amino acid sequence encoded by SEQ ID
NO:230.

SEQ ID NO:235 is the amino acid sequence encoded by SEQ ID
NO:231.

SEQ ID NO:236 is the amino acid sequence encoded by SEQ ID
NO:232.

20 SEQ ID NO:237 is GenBank Accession No. CAA58926

SEQ ID NO:238 is GenBank Accession No. BAA91327

SEQ ID NO:239 is GenBank Accession No. BAA22955

SEQ ID NO:240 is GenBank Accession No. NP_004258

SEQ ID NO:241 is GenBank Accession No. AAF61208

25 SEQ ID NO:242 is GenBank Accession No. CAA26370

SEQ ID NO:243 is the determined cDNA sequence for '56908.1

SEQ ID NO:244 is the determined cDNA sequence for '56909.1

SEQ ID NO:245 is the determined cDNA sequence for '56911.1

SEQ ID NO:246 is GenBank Accession No. AK000700

30 SEQ ID NO:247 is the determined cDNA sequence for '56912.1

SEQ ID NO:248 is GenBank Accession No. AB006624

SEQ ID NO:249 is the determined cDNA sequence for '56913.1

SEQ ID NO:250 is GenBank Accession No. NM_004267

SEQ ID NO:251 is the determined cDNA sequence for '56916.1

SEQ ID NO:252 is the determined cDNA sequence for '56917.1

SEQ ID NO:253 is the determined cDNA sequence for '56921.1

5 SEQ ID NO:254 is GenBank Accession No. AF216751

SEQ ID NO:255 is the determined cDNA sequence for '56922.1

SEQ ID NO:256 is GenBank Accession No. X02530

SEQ ID NO:257 is the determined cDNA sequence for '56923.1

SEQ ID NO:258 is the determined cDNA sequence for 54533.1

10 SEQ ID NO:259 is the determined cDNA sequence for 54534.1

SEQ ID NO:260 is the determined cDNA sequence for 54536.1

SEQ ID NO:261 is the determined cDNA sequence for 54538.1

SEQ ID NO:262 is the determined cDNA sequence for 54540.1

SEQ ID NO:263 is the determined cDNA sequence for 55084.1

15 SEQ ID NO:264 is the determined cDNA sequence for 55086.1

SEQ ID NO:265 is the determined cDNA sequence for 54555.1

SEQ ID NO:266 is the determined cDNA sequence for 54557.1

SEQ ID NO:267 is the determined cDNA sequence for 54564.1

SEQ ID NO:268 is the determined cDNA sequence for 55098.1

20 SEQ ID NO:269 is the determined cDNA sequence for 55473.1

SEQ ID NO:270 is the determined cDNA sequence for 55104.1

SEQ ID NO:271 is the determined cDNA sequence for 55105.1

SEQ ID NO:272 is the determined cDNA sequence for 55107.1

SEQ ID NO:273 is the determined cDNA sequence for 55108.1

25 SEQ ID NO:274 is the determined cDNA sequence for 55114.1

SEQ ID NO:275 is the determined cDNA sequence for 55477.1

SEQ ID NO:276 is the determined cDNA sequence for 55482.1

SEQ ID NO:277 is the determined cDNA sequence for 55483.1

SEQ ID NO:278 is the determined cDNA sequence for 55485.1

30 SEQ ID NO:279 is the determined cDNA sequence for 55487.1

SEQ ID NO:280 is the determined cDNA sequence for 55488.1

SEQ ID NO:281 is the determined cDNA sequence for 55087.1

SEQ ID NO:282 is the determined cDNA sequence for 55089.1
SEQ ID NO:283 is the determined cDNA sequence for 55092.1
SEQ ID NO:284 is the determined cDNA sequence for 55093.1
SEQ ID NO:285 is the determined cDNA sequence for 56926.1
5 SEQ ID NO:286 is the determined cDNA sequence for 56930.1
SEQ ID NO:287 is the determined cDNA sequence for 56944.1
SEQ ID NO:288 is the determined cDNA sequence for 56945.1
SEQ ID NO:289 is the determined cDNA sequence for 55490.1
SEQ ID NO:290 is the determined cDNA sequence for 55495.1
10 SEQ ID NO:291 is the determined cDNA sequence for 55504.1
SEQ ID NO:292 is the determined cDNA sequence for 55506.1
SEQ ID NO:293 is the determined cDNA sequence for 56480.1
SEQ ID NO:294 is the determined cDNA sequence for 56482.1
SEQ ID NO:295 is the determined cDNA sequence for 56484.1
15 SEQ ID NO:296 is the determined cDNA sequence for 56487.1
SEQ ID NO:297 is the determined cDNA sequence for 56488.1
SEQ ID NO:298 is the determined cDNA sequence for 56490.1
SEQ ID NO:299 is the determined cDNA sequence for 56493.1
SEQ ID NO:300 is the determined cDNA sequence for 56494.1
20 SEQ ID NO:301 is the determined cDNA sequence for 56495.1
SEQ ID NO:302 is the determined cDNA sequence for 56499.1
SEQ ID NO:303 is the determined cDNA sequence for 56517.1
SEQ ID NO:304 is the determined cDNA sequence for 56952.1
SEQ ID NO:305 is the determined cDNA sequence for 56953.1
25 SEQ ID NO:306 is the determined cDNA sequence for 56959.1
SEQ ID NO:307 is the determined cDNA sequence for 57139.1
SEQ ID NO:308 is the determined cDNA sequence for 57078.1
SEQ ID NO:309 is the determined cDNA sequence for 57092.1
SEQ ID NO:310 is the determined cDNA sequence for 57099.1
30 SEQ ID NO:311 is the determined cDNA sequence for 57100.1
SEQ ID NO:312 is the determined cDNA sequence for 57105.1
SEQ ID NO:313 is the determined cDNA sequence for 57111.1

SEQ ID NO:314 is the determined cDNA sequence for 57117.1
SEQ ID NO:315 is the determined cDNA sequence for 57121.1
SEQ ID NO:316 is the determined cDNA sequence for 57124.1
SEQ ID NO:317 is the determined cDNA sequence for 57125.1
5 SEQ ID NO:318 is the determined cDNA sequence for 54800.2
SEQ ID NO:319 is the determined cDNA sequence for 54802.2
SEQ ID NO:320 is the determined cDNA sequence for 54803.2
SEQ ID NO:321 is the determined cDNA sequence for 54805.2
SEQ ID NO:322 is the determined cDNA sequence for 54806.2
10 SEQ ID NO:323 is the determined cDNA sequence for 54809.2
SEQ ID NO:324 is the determined cDNA sequence for 54810.2
SEQ ID NO:325 is the determined cDNA sequence for 54813.2
SEQ ID NO:326 is the determined cDNA sequence for 54814.2
SEQ ID NO:327 is the determined cDNA sequence for 54816.2
15 SEQ ID NO:328 is the determined cDNA sequence for 54817.2
SEQ ID NO:329 is the determined cDNA sequence for 54819.2
SEQ ID NO:330 is the determined cDNA sequence for 54821.2
SEQ ID NO:331 is the determined cDNA sequence for 54823.2
SEQ ID NO:332 is the determined cDNA sequence for 54824.2
20 SEQ ID NO:333 is the determined cDNA sequence for 54825.2
SEQ ID NO:334 is the determined cDNA sequence for 54826.2
SEQ ID NO:335 is the determined cDNA sequence for 54827.2
SEQ ID NO:336 is the determined cDNA sequence for 54829.2
SEQ ID NO:337 is the determined cDNA sequence for 54830.2
25 SEQ ID NO:338 is the determined cDNA sequence for 54832.2
SEQ ID NO:339 is the determined cDNA sequence for 55800.2
SEQ ID NO:340 is the determined cDNA sequence for 55801.2
SEQ ID NO:341 is the determined cDNA sequence for 55803.2
SEQ ID NO:342 is the determined cDNA sequence for 55804.2
30 SEQ ID NO:343 is the determined cDNA sequence for 55805.2
SEQ ID NO:344 is the determined cDNA sequence for 55806.2
SEQ ID NO:345 is the determined cDNA sequence for 55808.2

SEQ ID NO:346 is the determined cDNA sequence for 55810.2
SEQ ID NO:347 is the determined cDNA sequence for 55811.2
SEQ ID NO:348 is the determined cDNA sequence for 55812.2
SEQ ID NO:349 is the determined cDNA sequence for 55814.2
5 SEQ ID NO:350 is the determined cDNA sequence for 55816.2
SEQ ID NO:351 is the determined cDNA sequence for 55817.2
SEQ ID NO:352 is the determined cDNA sequence for 55819.2
SEQ ID NO:353 is the determined cDNA sequence for 55820.2
SEQ ID NO:354 is the determined cDNA sequence for 55823.2
10 SEQ ID NO:355 is the determined cDNA sequence for 55824.2
SEQ ID NO:356 is the determined cDNA sequence for 55826.2
SEQ ID NO:357 is the determined cDNA sequence for 55828.2
SEQ ID NO:358 is the determined cDNA sequence for 55829.2
SEQ ID NO:359 is the determined cDNA sequence for 55831.2
15 SEQ ID NO:360 is the determined cDNA sequence for 55832.2
SEQ ID NO:361 is the determined cDNA sequence for 55833.2
SEQ ID NO:362 is the determined cDNA sequence for 55834.2
SEQ ID NO:363 is the determined cDNA sequence for 55835.2
SEQ ID NO:364 is the determined cDNA sequence for 55838.2
20 SEQ ID NO:365 is a predicted extended cDNA sequence for clone
48137 (L578S) having the isolated sequence of SEQ ID NO:89)
SEQ ID NO:366 is the predicted amino acid encoded by SEQ ID
NO:365
SEQ ID NO:367 is the determined cDNA sequence for 49949.5
25 SEQ ID NO:368 is the determined cDNA sequence for 49952.1
SEQ ID NO:369 is the determined cDNA sequence for 49956;contig 29
SEQ ID NO:370 is the determined cDNA sequence for 49960.4
SEQ ID NO:371 is the determined cDNA sequence for 49961;contig 21
SEQ ID NO:372 is the determined cDNA sequence for 49962.4
30 SEQ ID NO:373 is the determined cDNA sequence for 49962.5
SEQ ID NO:374 is the determined cDNA sequence for 49965.1
SEQ ID NO:375 is the determined cDNA sequence for 49966.1

SEQ ID NO:376 is the determined cDNA sequence for 49971.1
SEQ ID NO:377 is the determined cDNA sequence for 49975.1
SEQ ID NO:378 is the determined cDNA sequence for 49982.1
SEQ ID NO:379 is the determined cDNA sequence for 49986.1
5 SEQ ID NO:380 is the determined cDNA sequence for 49988.1
SEQ ID NO:381 is the determined cDNA sequence for 49993.1
SEQ ID NO:382 is the determined cDNA sequence for 49995.1
SEQ ID NO:383 is the determined cDNA sequence for 49996;contig 22
SEQ ID NO:384 is the determined cDNA sequence for 49999.1
10 SEQ ID NO:385 is the determined cDNA sequence for 50006;contig 23
SEQ ID NO:386 is the determined cDNA sequence for 50007.1
SEQ ID NO:387 is the determined cDNA sequence for 50009.3
SEQ ID NO:388 is the determined cDNA sequence for 50014.1
SEQ ID NO:389 is the determined cDNA sequence for 50016;contig 24
15 SEQ ID NO:390 is the determined cDNA sequence for 50017.1
SEQ ID NO:391 is the determined cDNA sequence for 50019.1
SEQ ID NO:392 is the determined cDNA sequence for 50022.1
SEQ ID NO:393 is the determined cDNA sequence for 50023.1
SEQ ID NO:394 is the determined cDNA sequence for 50024.1
20 SEQ ID NO:395 is the determined cDNA sequence for 50033.1
SEQ ID NO:396 is an extended cDNA sequence for SCC2-54 (SEQ ID
NO:178)
SEQ ID NO:397 is the amino acid sequence encoded by SEQ ID NO:396
SEQ ID NO:398 is the determined cDNA sequence for 56908.1
25 SEQ ID NO:399 is the determined cDNA sequence for 56911.1
SEQ ID NO:400 is the determined cDNA sequence for 56912.1
SEQ ID NO:401 is the determined cDNA sequence for 56913.1
SEQ ID NO:402 is the determined cDNA sequence for 56916.1
SEQ ID NO:403 is the determined cDNA sequence for 56917.1
30 SEQ ID NO:404 is the determined cDNA sequence for 56921.1
SEQ ID NO:405 is the determined cDNA sequence for 56922.1
SEQ ID NO:406 is the determined cDNA sequence for 56923.1

SEQ ID NO:407 is the determined cDNA sequence for 60974.1

SEQ ID NO:408 is the determined cDNA sequence for 60976.1

SEQ ID NO:409 is the determined cDNA sequence for 60977.1

SEQ ID NO:410 is the determined cDNA sequence for 60978.1

5 SEQ ID NO:411 is the determined cDNA sequence for 60980.1

SEQ ID NO:412 is an extended cDNA sequence for LSC-49 (SEQ ID
NO:29)

SEQ ID NO:413 is the amino acid sequence encoded by SEQ ID NO:412

10 SEQ ID NO:414 is an extended cDNA sequence for LSC-39 (SEQ ID
NO:26)

SEQ ID NO:415 is an extended cDNA sequence for LSC-46 (SEQ ID
NO:28)

SEQ ID NO:416 is an extended cDNA sequence for LSC-49 (SEQ ID
NO:29)

15 SEQ ID NO:417 is an extended cDNA sequence for LSC-51 (SEQ ID
NO:30)

SEQ ID NO:418 is an extended cDNA sequence for LSC-55 (SEQ ID
NO:32)

20 SEQ ID NO:419 is an extended cDNA sequence for LSC-64 (SEQ ID
NO:35)

SEQ ID NO:420 is an extended cDNA sequence for LSC-78 (SEQ ID
NO:42)

SEQ ID NO:421 is an extended cDNA sequence for LSC-103 (SEQ ID
NO:47)

25 SEQ ID NO:422 is an extended cDNA sequence for LSC-144 (SEQ ID
NO:53)

SEQ ID NO:423 is an extended cDNA sequence for LSC-148 (SEQ ID
NO:54)

30 SEQ ID NO:424 is an extended cDNA sequence for LSC-210 (SEQ ID
NO:74)

SEQ ID NO:425 is the amino acid sequence encoded by SEQ ID NO:414

SEQ ID NO:426 is the amino acid sequence encoded by SEQ ID NO:415

SEQ ID NO:427 is the amino acid sequence encoded by SEQ ID NO:416

SEQ ID NO:428 is the amino acid sequence encoded by SEQ ID NO:417

SEQ ID NO:429 is the amino acid sequence encoded by SEQ ID NO:418

SEQ ID NO:430 is the amino acid sequence encoded by SEQ ID NO:419

5 SEQ ID NO:431 is the amino acid sequence encoded by SEQ ID NO:420

SEQ ID NO:432 is the amino acid sequence encoded by SEQ ID NO:421

SEQ ID NO:433 is the amino acid sequence encoded by SEQ ID NO:422

SEQ ID NO:434 is the amino acid sequence encoded by SEQ ID NO:423

SEQ ID NO:435 is the amino acid sequence encoded by SEQ ID NO:424

10 SEQ ID NO:436 is the amino acid sequence encoded by a second open
reading frame (ORF-2) of clone SCC2-51, SEQ ID NO:175

SEQ ID NO:437 is the determined cDNA sequence for SCC2-16.

SEQ ID NO:438 is the determined cDNA sequence for SCC2-28.

SEQ ID NO:439 is the determined cDNA sequence for SCC2-62.

15 SEQ ID NO:440 is the determined cDNA sequence for SCC3-90.

DETAILED DESCRIPTION OF THE INVENTION

20 The present invention is directed generally to compositions and their use
in the therapy and diagnosis of cancer, particularly lung cancer. As described further
below, illustrative compositions of the present invention include, but are not restricted
to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such
polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and
immune system cells (*e.g.*, T cells).

25 The practice of the present invention will employ, unless indicated
specifically to the contrary, conventional methods of virology, immunology,
microbiology, molecular biology and recombinant DNA techniques within the skill of
the art, many of which are described below for the purpose of illustration. Such
techniques are explained fully in the literature. See, *e.g.*, Sambrook, et al. Molecular
30 Cloning: A Laboratory Manual (2nd Edition, 1989); Maniatis et al. Molecular Cloning:

- A Laboratory Manual (1982); DNA Cloning: A Practical Approach, vol. I & II (D. Glover, ed.); Oligonucleotide Synthesis (N. Gait, ed., 1984); Nucleic Acid Hybridization (B. Hames & S. Higgins, eds., 1985); Transcription and Translation (B. Hames & S. Higgins, eds., 1984); Animal Cell Culture (R. Freshney, ed., 1986); Perbal, A Practical Guide to Molecular Cloning (1984).

All publications, patents and patent applications cited herein, whether supra or infra, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise.

Polypeptide Compositions

As used herein, the term "polypeptide" is used in its conventional meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of this invention are amino acid subsequences comprising epitopes, *i.e.*, antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-232, 243-396, 398-412, 414-424 and 437-440, or a sequence that hybridizes under moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-232, 243-396, 398-412, 414-424 and 437-440. Certain illustrative polypeptides of the invention comprise amino acid sequences as set forth in any one of SEQ ID NOs: 229-232, 237-242, 397, 413 and 425-436.

The polypeptides of the present invention are sometimes herein referred to as lung tumor proteins or lung tumor polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in lung tumor samples. Thus, a "lung tumor polypeptide" or "lung tumor protein," refers
5 generally to a polypeptide sequence of the present invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed in a substantial proportion of lung tumor samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of lung tumor samples tested, at a level that is at least two fold, and preferably at least five fold,
10 greater than the level of expression in normal tissues, as determined using a representative assay provided herein. A lung tumor polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

15 In certain preferred embodiments, the polypeptides of the invention are immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with lung cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as
20 those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

25 As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide.
30 Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for

the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and
5 antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of
10 the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic
15 activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids),
20 relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may also comprise one or more polypeptides that are immunologically reactive with T cells and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic
25 fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in
30 the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide compositions set forth herein, such as those set forth in SEQ ID NOs: 229-232, 237-242, 397, 413 and 425-436, or those
5 encoded by a polynucleotide sequence set forth in a sequence of SEQ ID NOs: 1-232, 243-396, 398-412, 414-424 and 437-440.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally encompassed by the present invention will typically exhibit at least about 70%, 75%,
10 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity (determined as described below), along its length, to a polypeptide sequences set forth herein.

In one preferred embodiment, the polypeptide fragments and variants provide by the present invention are immunologically reactive with an antibody and/or
15 T-cell that reacts with a full-length polypeptide specifically set for the herein.

In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or more of that exhibited by a full-length polypeptide sequence specifically set forth
20 herein.

A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of
25 the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein and/or using any of a number of techniques well known in the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader
30 sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide with desirable characteristics, e.g., with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE 1

Amino Acids			Codons						
Alanine	Ala	A	GCA	GCC	GCG	GCU			
Cysteine	Cys	C	UGC	UGU					
Aspartic acid	Asp	D	GAC	GAU					
Glutamic acid	Glu	E	GAA	GAG					
Phenylalanine	Phe	F	UUC	UUU					
Glycine	Gly	G	GGA	GGC	GGG	GGU			
Histidine	His	H	CAC	CAU					
Isoleucine	Ile	I	AUA	AUC	AUU				
Lysine	Lys	K	AAA	AAG					
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU	
Methionine	Met	M	AUG						
Asparagine	Asn	N	AAC	AAU					
Proline	Pro	P	CCA	CCC	CCG	CCU			
Glutamine	Gln	Q	CAA	CAG					
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU	
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU	
Threonine	Thr	T	ACA	ACC	ACG	ACU			
Valine	Val	V	GUA	GUC	GUG	GUU			
Tryptophan	Trp	W	UGG						
Tyrosine	Tyr	Y	UAC	UAU					

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are:

isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (−0.4); threonine (−0.7); serine (−0.8); tryptophan (−0.9); tyrosine (−1.3); proline (−1.6); histidine (−3.2); glutamate (−3.5); glutamine (−3.5); aspartate (−3.5); asparagine (−3.5); lysine (−3.9); and arginine (−4.5).

5 It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5
10 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with a biological property of the protein.

15 As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 \pm 1); glutamate (+3.0 \pm 1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (−0.4); proline (−0.5 \pm 1); alanine (−0.5); histidine (−0.5); cysteine (−1.0); methionine (−1.3); valine (−1.5); leucine (−1.8); isoleucine (−1.8); tyrosine (−
20 2.3); phenylalanine (−2.5); tryptophan (−3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even
25 more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that take various of the foregoing characteristics into consideration are well known to those
30 of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of
5 nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic
10 nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may
15 represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or
20 alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally
25 directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be
30 "identical" if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison

window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent

sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted
5 when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

10 In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference
15 sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by
20 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes
25 (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to
30 desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and

transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein
5 capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see*, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12
10 fragment. Ra12 compositions and methods for their use in enhancing the expression and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid.
15 MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; *see also*, Skeiky et al., *Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding
20 sequence express at high levels and remain as a soluble polypeptides throughout the purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous immunogenic polypeptides with which it is fused. One preferred Ra12 fusion polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally
25 comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a
30 sequence. Ra12 polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide

comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a portion thereof.

5 Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred
10 embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1
15 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

 In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine
20 amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for
25 expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

30 Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as

described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention, when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4⁺ T-cells specific for the polypeptide.

5 Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are
10 synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and
15 may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of the invention are isolated. An "isolated" polypeptide is one that is removed from its original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural
20 system. Preferably, such polypeptides are also purified, *e.g.*, are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure.

Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide
25 compositions. The terms "DNA" and "polynucleotide" are used essentially interchangeably herein to refer to a DNA molecule that has been isolated free of total genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large
30 chromosomal fragments or other functional genes or polypeptide coding regions. Of

course, this refers to the DNA molecule as originally isolated, and does not exclude genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably and immunogenic variant or derivative, of such a sequence.

Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-232, 243-396, 398-412, 414-424 and 437-440, complements of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-232, 243-396, 398-412, 414-424 and 437-440, and degenerate variants of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-232, 243-396, 398-412, 414-424 and 437-440. In certain preferred embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NOs: 1-232, 243-396, 398-412, 414-424 and 437-440, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a

polynucleotide sequence of this invention using the methods described herein, (e.g., BLAST analysis using standard parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into
5 account codon degeneracy, amino acid similarity, reading frame positioning and the like.

Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished
10 relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompass homologous genes of xenogenic origin.

In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of
15 sequence identical to or complementary to one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate
20 lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103, *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.

In another embodiment of the invention, polynucleotide compositions are
25 provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides
30 include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in

the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, *e.g.*, polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a

reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for

nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not,

have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25 nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded

plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known rules of complementary base pairing (see, for example, Watson, 1987). Typically,

vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

5 In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

10 In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 nucleotide long contiguous sequence that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence
15 disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

 The ability of such nucleic acid probes to specifically hybridize to a
20 sequence of interest will enable them to be of use in detecting the presence of complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

 Polynucleotide molecules having sequence regions consisting of
25 contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in
30 various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in

hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

5 The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules
10 obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

 Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth
15 herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various factors. For example, one may wish to employ primers from towards the termini of the total sequence.

20 Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCR™ technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing
25 selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

 The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or
30 gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity,

one will typically desire to employ relatively stringent conditions to form the hybrids, e.g., one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate
5 little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be
10 needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered
15 more stringent by the addition of increasing amounts of formamide, which serves to destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

According to another embodiment of the present invention,
20 polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis
25 is well established. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1,
30 striatal GABA_A receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent

5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

5 Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or
10 derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In each case, preferred compositions comprise a sequence region that is complementary, and more preferably substantially-complementary, and even more preferably,
15 completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure, T_m , binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that
20 would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis
25 software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997, 25(17):3389-402).

 The use of an antisense delivery method employing a short peptide vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic
30 domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered

into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, *Proc Natl Acad Sci U S A.* 1987 Dec;84(24):8788-92; Forster and Symons, *Cell.* 1987 Apr 24;49(2):211-20). For example, a large number of ribozymes accelerate phosphoester transfer reactions with a high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et al.*, *Cell.* 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, *J Mol Biol.* 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, *Nature.* 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme

necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity
5 of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action (Woolf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the
10 specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis δ virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are
15 described by Rossi *et al.* Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel *et al.*, Nucleic Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis δ virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec
20 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada *et al.*, Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is
25 described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be
30 limited to specific motifs mentioned herein.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically

incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

5 Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO 92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat.
10 Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the
15 general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be
20 directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter; infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical,
25 systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s)
30 within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase

III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the
5 prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as
10 retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number methods that
15 traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences
20 that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal
25 phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-500; Hanvey *et al.*, *Science*. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, *Bioorg Med Chem.* 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a
30 stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45). The manual protocol lends itself to the
5 production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines
10 can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of
15 peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The
20 ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*,
25 Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*, Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997
30 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in

diagnostics, modulating protein in organisms, and treatment of conditions susceptible to therapeutics.

Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

Polynucleotide Identification, Characterization and Expression

Polynucleotides compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by

reference in its entirety. Briefly, in PCR™, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse transcription and PCR™ amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCR™ amplification technique, are readily known and available in the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat. Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara, 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (*e.g.*, a tumor cDNA library)

using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes.

5 Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe
10 (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and
15 partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can then be assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

20 Alternatively, amplification techniques, such as those described above, can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and
25 used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known
30 region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or

RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous in some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide

sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or
5 recombinant nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding
10 sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical
15 methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo
20 Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (e.g., Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be
25 confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

In order to express a desired polypeptide, the nucleotide sequences
30 encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, i.e., a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well

known to those skilled in the art may be used to construct expression vectors containing sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) *Current Protocols in Molecular Biology*, John Wiley & Sons, New York. N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (*e.g.*, baculovirus); plant cell systems transformed with virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (*e.g.*, Ti or pBR322 plasmids); or animal cell systems.

The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used. For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSFORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example, when large quantities are needed, for example for the induction of antibodies, vectors

which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of .beta.-galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods Enzymol.* 153:516-544.

In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, *Autographa californica* nuclear polyhedrosis virus

(AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91 :3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the

desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as
5 CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a
10 polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer
15 resistance to selection, and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine
20 kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or aprt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which
25 confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in
30 place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate

luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that
5 the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter.
10 Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-
15 RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies
20 specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed.
25 These and other assays are described, among other places, in Hampton, R. et al. (1990; *Serological Methods, a Laboratory Manual*, APS Press, St Paul, Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means
30 for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions

thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant (K_d) of the interaction, wherein a smaller K_d represents a greater affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both the "on rate constant" (K_{on}) and the "off rate constant" (K_{off}) can be determined by calculation of the concentrations and the actual rates of association and dissociation.

The ratio of K_{off}/K_{on} enables cancellation of all parameters not related to affinity, and is

thus equal to the dissociation constant K_d . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable regions" which are interposed between more conserved flanking stretches known as "framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients with and without a cancer, such as lung cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.,* mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.,* reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine,

aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

5 Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by
10 conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

 A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding
15 properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab')₂" fragment which comprises both antigen-binding sites. An "Fv" fragment
20 can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V_H::V_L heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule.
25 Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

 A single chain Fv ("sFv") polypeptide is a covalently linked V_H::V_L heterodimer which is expressed from a gene fusion including V_H- and V_L-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci.
30 USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will

fold into a three dimensional structure substantially similar to the structure of an antigen-binding site. See, *e.g.*, U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRs and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (*e.g.*, a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRs. Within FRs, certain amino residues and certain structural features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical" structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including

chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) Nature 349:293-299; Lobuglio et al. (1989) Proc. Nat. Acad. Sci. USA 86:4220-4224; Shaw et al. (1987) J Immunol. 138:4534-4538; and Brown et al. (1987) Cancer Res. 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) Nature 332:323-327; Verhoeyen et al. (1988) Science 239:1534-1536; and Jones et al. (1986) Nature 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, *e.g.*, a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) Ann. Rev. Biochem. 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (*e.g.*, solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V

region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (*e.g.*, electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In

another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the

generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator

cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

5 Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

10 It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target
15 cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

20 Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide
25 and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination
30 with one or more immunostimulants.

It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (*e.g.*, salts of
5 primary, secondary and tertiary amines and basic amino acids) and inorganic bases (*e.g.*, sodium, potassium, lithium, ammonium, calcium and magnesium salts).

In another embodiment, illustrative immunogenic compositions, *e.g.*, vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As
10 noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary
15 regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

Therefore, in certain embodiments, polynucleotides encoding
20 immunogenic polypeptides described herein are introduced into suitable mammalian host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using
25 techniques known in the art. The recombinant virus can then be isolated and delivered to a subject. A number of illustrative retroviral systems have been described (*e.g.*, U.S. Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin
30 (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses

persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) J. Virol. 57:267-274; Bett et al. (1993) J. Virol. 67:5911-5921; Mittereder et al. (1994) Human Gene Therapy 5:717-729; Seth et al. (1994) J. Virol. 68:933-940; Barr et al. (1994) Gene Therapy 1:51-58; Berkner, K. L. (1988) BioTechniques 6:616-629; and Rich et al. (1993) Human Gene Therapy 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using techniques well known in the art. See, *e.g.*, U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) Molec. Cell. Biol. 8:3988-3996; Vincent et al. (1990) Vaccines 90 (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) Current Opinion in Biotechnology 3:533-539; Muzyczka, N. (1992) Current Topics in Microbiol. and Immunol. 158:97-129; Kotin, R. M. (1994) Human Gene Therapy 5:793-801; Shelling and Smith (1994) Gene Therapy 1:165-169; and Zhou et al. (1994) J. Exp. Med. 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. Homologous recombination serves to insert the vaccinia promoter plus the gene encoding the polypeptide of interest into the viral genome. The resulting TK.sup.(-) recombinant can be selected by culturing the cells in the presence of 5-bromodeoxyuridine and picking viral plaques resistant thereto.

A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or coexpression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected in vitro with a vaccinia virus recombinant that encodes the bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in

that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, *e.g.*, Elroy-Stein and Moss, *Proc. Natl. Acad. Sci. USA* (1990) 87:6743-6747; Fuerst et al. *Proc. Natl. Acad. Sci. USA* (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, *e.g.*, WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242;

WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

5 In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in the specific location and orientation via homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the polynucleotide may be stably maintained in the cell as a separate, episomal segment of
10 DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression construct employed.

15 In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

20 In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK) and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in
25 U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device, propelling the particles into a target tissue of interest.

30 In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described

in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Within certain embodiments of the invention, the adjuvant composition is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL[®] adjuvants are available from Corixa Corporation (Seattle, WA; *see*, for example, US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example combinations of at least two of the following group comprising QS21, QS7, Quil A, β -escin, or digitonin.

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix, particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol^R to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

In one preferred embodiment, the adjuvant system includes the combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL[®] adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in

WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-MPL[®] adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

5 Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical
10 compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhanzyn[®]) (Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described
15 in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula

20 (I): $\text{HO}(\text{CH}_2\text{CH}_2\text{O})_n\text{-A-R}$,

wherein, n is 1-50, A is a bond or $-\text{C}(\text{O})-$, R is C_{1-50} alkyl or Phenyl C_{1-50} alkyl.

One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein n is between 1 and 50, preferably 4-24, most preferably 9; the R component is C_{1-50} ,
25 preferably $\text{C}_4\text{-C}_{20}$ alkyl and most preferably C_{12} alkyl, and A is a bond. The concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether.
30 Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck

index (12th edition: entry 7717). These adjuvant molecules are described in WO 99/52549.

The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant
5 combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be
10 engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs,
15 including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to
20 be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T
25 cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600,
30 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of
5 cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation,
10 maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are
15 characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules
20 (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells
25 may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun
30 approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or

RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated
5 immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration,
10 including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release.
15 In other embodiments, however, a more rapid rate of release immediately upon administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers
20 include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends
25 upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (*e.g.*, polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S.
30 Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763; 5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems, such as described in WO/99 40934, and references cited therein, will also be useful for

many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

5 The pharmaceutical compositions of the invention will often further comprise one or more buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that
10 render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

 The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers
15 are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

20 The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

25 In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

30 The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature

1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia, cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds may be incorporated into sustained-release preparation and formulations.

Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of active compound(s) in each therapeutically useful composition may be prepared in such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

For oral administration the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants.

Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even
5 intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be
10 prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous
15 preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium
20 containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or by the use of surfactants. The prevention of the action of microorganisms can be
25 facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate
30 and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered

isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one
5 dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of
10 course preferably meet sterility, pyrogenicity, and the general safety and purity standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free
15 amino groups of the protein) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine,
20 trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption
25 delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase
30 "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the lungs *via* nasal aerosol sprays has been described, *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as potential drug carriers is generally known to those of skill in the art (see for example, Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998 Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of

liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)).

Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 μm) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

Cancer Therapeutic Methods

In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of lung cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous

host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies

have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free

survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples
5 obtained from a patient before and after treatment.

Cancer Detection and Diagnostic Compositions, Methods and Kits

In general, a cancer may be detected in a patient based on the presence of one or more lung tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies)
10 obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as lung cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of
15 mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a lung tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g.,
20 Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

25 In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a
30 binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G,

protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length lung tumor proteins and polypeptide portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μ g, and preferably about 100 ng to about 1 μ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports

having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

5 In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody
10 complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

 More specifically, once the antibody is immobilized on the support as
15 described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as
20 phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.,* incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of
25 ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

 Unbound sample may then be removed by washing the solid support
30 with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed
5 and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different
10 reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as lung cancer,
15 the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three
20 standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot
25 of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered
30 positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In

general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a

polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous
5 nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989*).

10 One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification
15 may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered
20 positive.

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be
25 performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

30 Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such

binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLE 1USE OF MOUSE ANTISERA TO IDENTIFY cDNA SEQUENCES ENCODING
LUNG TUMOR ANTIGENS

5 This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by screening of lung tumor cDNA libraries with mouse anti-tumor sera.

 A small cell cDNA lung tumor expression library was constructed using mRNA from the small cell carcinoma cell line NCIH69 employing the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Mouse anti-SCID mouse serum
10 was developed by growing the lung small cell carcinoma cell lines NCIH69 and NCIH128 in SCID mice, removed SCID serum containing shed and secreted tumor antigens. These sera were pooled and injected into normal mice to produce anti-lung carcinoma serum. The antiserum was adsorbed with *E. coli* lysate and human GAPDH protein, and human PBMC lysate was added to the serum to block antibody to proteins
15 found in normal tissue. The cDNA expression library was then screened with this anti-serum using a goat anti-mouse IgG-A-M (H+L) alkaline phosphatase second antibody developed with NBT/BCIP (Gibco BRL Labs., Gaithersburg, MD). Phage was purified and phagemid excised for clones with inserts in a pBK-CMV vector for expression in prokaryotic or eukaryotic cells.

20 The determined cDNA sequences for 76 isolated clones are provided in SEQ ID NO:1-76. Comparison of these sequences with those in the public database as described above, revealed no significant homologies to SEQ ID NO:7, 14, 21, 46 and 55. SEQ ID NO:11, 16, 20, 41, 49 and 74 were found to show some homology to previously identified expressed sequence tags (ESTs). The remaining clones were
25 found to show some degree of homology to previously identified genes. The expression levels of certain of the isolated antigens in lung tumor tissues compared to expression levels in 36 normal tissues was determined by microarray technology. The results of these studies are shown below in Table 2, together with the database analyses for these sequences.

Table 2

Clone Name	SEQ ID NO:	Description	Lung Tumor Over-Expression (≥ 2)			
			LT+F/N	SCC+M/N	Squa/N	Aden/N
LSC-2	2	CDM, 6C6, BAP31/2	-	-	2.4	-
LSC-6	5	Motor protein p87/89	-	2.2	-	-
LSC-7	6	Ku autoantien 70 kDa	-	2.2	2.3	-
LSC-10	8	PIBF1 protein	-	2.4	-	-
LSC-11	9	Ku autoantien 70 kDa	-	2.4	-	-
LSC-15	11	Novel	-	-	2.9	-
LSC-29	19	Unknown DKFZp586N1020	-	2.5	-	-
LSC-33	22	10 methylene 4 hydrofolate DH	-	2.4	-	-
LSC-39	26	P1 protein	2.4	5.0	2.8	-
LSC-43	27	Minichrom maint deficient	2.3	7.1	2.8	-
LSC-46	28	Non-metastatic cell 1 NME1	2.6	2.5	2.7	2.1
LSC-49	29	GTPase act. Pro. ID- GAP	3.6	10.0	3.8	3.2
LSC-51	30	ZIC family member 2	-	3.4	-	-
LSC-55	32	Transmembrane(63 kDa) ER	2.7	2.2	4.2	2.3
LSC-64	35	Macrophage Migr Inhib Fac	2.6	3.2	3.9	-
LSC-72	38	hRif beta (p102 protein)	2.4	7.0	2.6	-
LSC-76	40	Pro Synth Init. Factor	-	-	-	2.1
LSC-78	42	Motor protein p87/89	-	2.7	2.2	-
LSC-81	43	Epidermal GFR subst 8 EPS8	-	-	2.7	2.1
LSC-101	45	Transmembrane(63 kDa) ER	2.7	-	4.3	-
LSC-103	47	Nuclear factor 4	-	4.3	2.8	-
LSC-134	51	Fumarase	-	3.6	-	-
LSC-142	52	Unknown BAC CTA363M4	-	-	2.5	-
LSC-144	53	Accessory Pro BAP31/BAP2	2.5	-	2.9	2.4
LSC-148	54	Unknown DKFZp586N1020	-	2.2	-	-
LSC-149	55	Novel / Novel	2.6	2.4	3.1	3.5
LSC-163	57	Unknown Ch8p11.2 sect2/19	-	-	-	2.4

LSC-170	58	Unknown PAC DJ0777023	2.2	3.0	2.2	-
LSC-210	74	Novel	-	2.6	2.1	-

LT+F/N = Lung Tumor plus Fetal tissue over Normal tissues

SC+M/N = Lung Small Cell carcinoma plus Metastatic over Normal tissues

Squa/N = Squamous lung tumor over Normal tissues

5 Aden/N = Adenocarcinoma over Normal tissues

EXAMPLE 2

ISOLATION OF LUNG TUMOR cDNA SEQUENCES

BY CONVENTIONAL SUBTRACTION

10 A human lung squamous cell carcinoma cDNA expression library was constructed from poly A⁺ RNA from a pool of two patient tissues using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD) following the manufacturer's protocol. Specifically, lung carcinoma tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was
15 extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using an oligo dT cellulose column as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with
20 BstXI/EcoRI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with cDNA size fractionation columns (BRL Life Technologies), the cDNA was ligated into the BstXI/NotI site of pcDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human lung cDNA expression
25 library was prepared from a pool of normal lung, kidney, colon, pancreas, brain, resting PBMC, heart, skin and esophagus, with esophagus cDNAs making up one third of the material. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA

cDNA library subtraction was performed using the above lung squamous
30 cell carcinoma and normal cDNA library, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a lung squamous cell carcinoma-specific subtracted cDNA library was generated as follows. To from the driver cDNA,

normal tissue cDNA library (80 µg) was digested with BamHI and XhoI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 133 µl of H₂O, heat-denatured and mixed with 133 µl (133 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (67 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H₂O to form the driver DNA.

To form the tracer DNA, 10 µg lung squamous cell carcinoma cDNA library was digested with NotI and SpeI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech, Palo Alto, CA). Typically, 5 µg of cDNA was recovered after the sizing column. Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into NotI/SpeI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a lung squamous cell carcinoma specific subtracted cDNA library (referred to as LST-69).

A cDNA library (referred to as mets3616A) was constructed from a metastatic lung adenocarcinoma. The mets3616A cDNA library was subtracted against a cDNA library prepared from a pool of normal lung, liver, pancreas, skin, kidney, brain and resting PBMC. To increase the specificity of the subtraction, the driver was spiked with genes that were determined to be most abundant in the mets3616A cDNA library, such as EF1-alpha, integrin-beta and anticoagulant protein PP4, as well as with cDNAs

that were previously found to be differentially expressed in subtracted lung adenocarcinoma cDNA libraries. The resulting subtracted library was referred to as mets3616A-S1.

The expression levels of 831 cDNAs from LST-S6 and 521 cDNAs from
5 Mets3616A-S1 in lung tumor tissue and normal tissues was analyzed by microarray technology (Synteni, Palo Alto, CA). Briefly, the cDNAs were PCR amplified and the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were
10 generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Thirty-four non-redundant cDNA clones showed 5-fold over-expression in lung tumors, compared with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine,
15 kidney, stomach, brain, small intestine, bladder and salivary gland). The determined cDNA sequences for the 34 isolated clones are provided in SEQ ID NO:77-110.

These sequences were compared to known sequences in the gene bank using the EMBL and GenBank databases. The sequences of SEQ ID NO:77, 86, 90 and 108 were found to show some homology to previously identified expressed sequence
20 tags (ESTs). The sequences of SEQ ID NO:78-85, 87-89, 91-107 and 109-110 were found to show some homology to previously identified genes.

The determined cDNA sequences of 54 clones isolated from lung tumor cDNA libraries that were shown to be differentially over-expressed in non-small cell lung carcinoma by are provided in SEQ ID NO:111-142 and 367-395.

25

EXAMPLE 3

USE OF PATIENT SERA TO IDENTIFY DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS

30 This example illustrates the isolation of cDNA sequences encoding lung tumor antigens by expression screening of lung tumor samples with autologous patient sera.

A cDNA expression library was prepared using mRNA from the lung small cell carcinoma cell line NCIH69 in the lambda ZAP Express expression vector (Stratagene) as described above, and screened with a pool of lung small cell carcinoma patient sera. The sera pool was adsorbed with *E. coli* lysate and human PBMC lysate was added to the serum to block antibody to proteins found in normal tissue. Screening was performed as described in Sambrook et al., (*Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989), with the secondary antibody being goat anti-human IgG-A-M (H + L) conjugated with alkaline phosphatase, developed with NBT/BCIP (Gibco BRL). Positive plaques expressing immunoreactive antigens were purified. Phagemid from the plaques was rescued and the nucleotide sequences of the clones was determined.

The determined cDNA sequences of 86 isolated clones are provided in SEQ ID NO:143-228. The sequences of SEQ ID NO:153, 154, 163, 178, 186, 202, 203, 218 and 219 were found to show some homology to previously identified ESTs. The sequences of SEQ ID NO:143-152, 155-162, 164-177, 179-185, 187-201, 204-217 and 220-228 were found to show some homology to previously isolated genes. The sequences of an additional three isolated clones (referred to as SCC2-16, SCC2-28 and SCC2-620 are provided in SEQ ID NO:437-439.

The expression levels of certain of the isolated antigens in lung tumor tissues compared to expression levels in 36 normal tissues was determined using microarray technology and computer analysis. The results of these studies are shown below in Table 3, together with the database analyses for these sequences.

Table 3

Clone Name	SEQ ID NO:	Description	Lung Tumor Over-Expression (≥ 2)			
			LT+F/N	SC+M/N	Squa/N	Aden/N
SCC2-5	146	Unknown KIAA0878	-	3.2	-	2.2
SCC2-9	148	Tubulin K-alpha-1	-	2.2	-	-
SCC2-10	149	NY-REN-64 (pro kinase)	2.0	14.8	3.5	-
SCC2-11	150	TBP-assoc. fact. 2-170	-	5.4	-	-
SCC2-13	152	Centromere Pro F (CENPF)	2.3	5.4	2.8	-
SCC2-14	153	BRUNOL-4	2.7	9.4	3.1	2.3

SCC2-16	437	Non metastatic cells 2	2.3	2.1	2.7	-
SCC2-17	154	Novel (V87915)	2.0	-	2.8	-
SCC2-20	156	Cytoplas Linker Pro 170a2	2.1	3.0+	2.8	-
SCC2-23	157	Hypoxia-induc fact 1 a	2.2	3.0	2.7	-
SCC2-24	158	Actin gamma 1	-	3.8	2.0	-
SCC2-28	438	CHORD-containing pro 1	-	2.1	-	-
SCC2-29	160	Unk. DJ0669I17; ALR-like	2.2	4.0	3.0	2.2
SCC2-31	162	Unknown chrom 1	2.2	3.4	2.8	-
SCC2-36	165	Unknown (T20633)	3.3	2.6	5.5	3.4
SCC2-37	166	Sex-det reg Y Box 21 SOX 2	-	3.0	-	-
SCC2-43	170	CHORD-containing pro 1	-	2.1	-	-
SCC2-50	231	Hypoxia-induc fact 1 a	6.0	3.9	13.7	5.0
SCC2-51	175	Unknown KIAA1051	2.1	3.6	2.0	-
SCC2-54	178	Unknown FLJ20725	-	2.4	2.1	-
SCC2-60	181	Unknown Cosmid R32889	-	3.2	-	-
SCC2-62	439	CHORD-containing pro 1	-	2.1	-	-
SCC2-66	183	Novel, similar to transferase	-	2.2	-	-
SCC2-68	184	Ribosomal pro S7 (RPS7)	-	2.2	-	-

LT+F/N = Lung Tumor plus Fetal tissue over Normal tissues

SC+M/N = Lung Small Cell carcinoma plus Metastatic over Normal tissues

Squa/N = Squamous lung tumor over Normal tissues

5 Aden/N = Adenocarcinoma over Normal tissues

10 The expression levels of certain other of the isolated antigens in lung tumor tissues compared to expression levels in 36 normal tissues was determined using microarray technology and either computer or visual analysis. The results of these studies are shown below in Table 4, together with the databank analyses for these sequences. These results indicate that these antigens are over-expressed in lung tumor tissue compared to normal tissue.

Table 4

Clone Name	SEQ ID NO:	Description	Ratio T/N Mean/Med
SCC2-58	180	Sox-2	visual
SCC2-79	190	Mixed-lineage leukemia 4 / AF-6	2.0/2.0 sq
SCC2-91	194	Hepatocellular carcinoma-assoc Ag 58	visual
SCC2-100	200	F-Box protein FBW2	visual
SCC2-102	202	Novel	visual
SCC2-104	204	MAP-kinase act death domain MADD	visual
SCC2-143	214	Unknown HSPC232	2.8/2.1 sq
SCC2-266	226	HMG-2	visual

5 Ratio T/N = lung tumor tissues over normal tissues

EXAMPLE 4

CLONING OF cDNAs ENCODING LUNG SMALL CELL CARCINOMA ANTIGENS

10 Lung small cell carcinoma antigens were cloned by screening a small cell
cDNA expression library with a mouse anti-SCID mouse serum. This antiserum was
developed by growing lung small cell carcinoma cell lines NCIH69 and NCIH128 in
SCID mice, removing SCID serum containing shed and secreted tumor antigens and
immunizing normal mice with this serum. The library was constructed with mRNA
15 from cell line NCIH128 in the lambda ZAP Express expression vector (Stratagene).
The antiserum was adsorbed with *E. coli* lysate and human GAPDH protein and Ku
autoantigens, and human PBMC lysate was added to the serum to block antibody to
proteins found in normal tissue. Table 5 lists the data bank analyses for the nucleotide
sequences. The determined cDNA sequences of the clones are provided in SEQ ID
20 NO:258-317.

Table 5

SEQ ID NO.:	Clone ID #	Genbank Homologies
258	54533	Novel
259	54534	Homo sapiens mRNA for LAK-1
260	54536	Homo sapiens CGI-108 protein mRNA
261	54538	Human mRNA for HHR23A protein
262	54540	Homo sapiens chromosome 17, clone hRPC. 1030_0_14
263	55084	Homo sapiens homolog of rat elongation factor p18 (p18)
264	55086	Homo sapiens HSPC194 mRNA
265	54555	Homo sapiens accessory proteins BAP31/BAP29 (DXS1357E) mRNA
266	54557	Homo sapiens mesenchymal stem cell protein DSCD75 mRNA
267	54564	Homo sapiens prp28, U5 snRNP 100 kd protein (U5-100K) mRNA
268	55098	Novel
269	55473	Homo sapiens uroporphyrinogen III synthase (congenital erythropoietic porphyria) (UROS)
270	55104	Homo sapiens carbonyl reductase (LOC51181)
271	55105	Homo sapiens membrane component, chromosome 11, surface marker 1 (M11S1)
272	55107	H.sapiens mRNA encoding GPI-anchored protein p137
273	55108	Novel
274	55114	Homo sapiens mRNA; cDNA DKFZp56401716
275	55477	H.sapiens YB-1 gene promoter region
276	55482	Homo sapiens mRNA ; cDNA DKFZp434B0425
277	55483	Human Gu protein mRNA
278	55485	Homo sapiens 45kDa splicing factor mRNA
279	55487	Homo sapiens genomic DNA, chromosome 21q, section 72/105
280	55488	Homo sapiens chromosome 17, clone hCIT529110
281	55087	Novel (partial overlap of Unknown: Homo sapiens partial mRNA, clone c1-10e16)
282	55089	Homo sapiens scaffold attachment factor A (SAF-A) mRNA
283	55092	Homo sapiens density regulated protein drp1 mRNA
284	55093	H.sapiens mRNA encoding GPI-anchored protein p137
285	56926	Homo sapiens high-mobility group (nonhistone chromosomal) protein 17 (HMG17)
286	56930	Novel
287	56944	Homo sapiens KBNA-2 co-activator (100kD) (p100), mRNA
288	56945	Novel
289	55490	Homo sapiens death-associated protein 6 (DAXX) mRNA, and translated products.

SEQ ID NO:.	Clone ID #	Genbank Homologies
290	55495	Homo sapiens mRNA for MEGF6
291	55504	Mus musculus hairy / enhancer of split 6 mRNA
292	55506	Novel / (136bp: Mus musculus mRNA for Rab24 protein)
293	56480	Novel
294	56482	H.sapiens DNA from chromosome 19-cosmids R31158, R31874, & R28125, genomic seq.
295	56484	Novel
296	56487	Human L23 mRNA for putative ribosomal protein
297	56488	Homo sapiens cDNA FLJ10526 fis, clone NT2RP2000931, highly similar to MATRIN 3
298	56490	Homo sapiens Sul1 isolog mRNA
299	56493	Novel
300	56494	Homo sapiens mRNA; cDNA DKFZp564B167 (from clone DKFZp564B167)
301	56495	Homo sapiens 12p13.3 BAC RPC111-543P15 (Roswell Park Cancer Inst. Human BAC lib.)
302	56499	Human DNA-binding protein B (dbpB) gene, 3' end
303	56517	Homo sapiens esterase D mRNA
304	56952	Homo sapiens 14q32 Jagged2 gene, complete cds; and unknown gene
305	56953	Homo sapiens DNA polymerase zeta catalytic subunit (REV3L) mRNA
306	56959	Novel
307	57139	Homo sapiens ribosomal protein, large, PO (RPLPO) mRNA
308	57078	Homo sapiens alpha-tubulin isoform 1 mRNA
309	57092	Novel
310	57099	Homo sapiens uncharacterized hypothalamus protein HBEX2 mRNA
311	57100	Novel (last 120 bp: Unknown: Canine 21 kDa Signal peptase subunit mRNA)
312	57105	Homo sapiens splicing factor, arginine/serine-rich 7 (35kD) (SFRS7)
313	57111	Human chromosome 14 DNA sequence
314	57117	Human DNA sequence from cosmid V857G56, between markers DXS366 and DXS87 on chromosome X contains ESTs
315	57121	Homo sapiens genomic DNA of 8p21.3-p22 anti-oncogene of hepatocellular colorectal and non-small cell lung cancer, segment 3/11
316	57124	H.sapiens MLN50 mRNA
317	57125	Homo sapiens calreticulin (CALR) , mRNA

EXAMPLE 5

cDNAs ENCODING LUNG SMALL CELL CARCINOMA ANTIGENS

Lung small cell carcinoma antigens were cloned by screening a small cell
 5 cDNA library (NCIH 128) with small cell carcinoma patient sera. The library was
 constructed with mRNA from cell line NICH 128 in the lambda ZAP Express expression
 vector (Stratagene). The antiserum was adsorbed with *E. coli* lysate and human
 GAPDH protein, and human PBMC lysate was added to the serum to block antibody to
 proteins found in normal tissue. Table 6 lists the homologies identified by database
 10 analyses for nucleotide sequences shown in SEQ ID NO:318-364. An additional
 isolated cDNA sequence (referred to as SCC3-90) is provided in SEQ ID NO:440.

Table 6

SEQ ID NO:	Clone ID #	Genbank Homologies
318	54800	Human Ig germline H-chain G-E-A region B
319	54802	Human mRNA for T-cell cyclophilin
320	54803	Unknown BAC clone GS1-11E15
321	54805	Unknown Homo sapiens cDNA FLJ20272 fis
322	54806	Unknown Homo sapiens mRNA for KIAA0713 protein
323	54809	Unknown Homo sapiens mRNA for RIE2 sid2705
324	54810	Homo sapiens glutamyl-prolyl-tRNA synthetase
325	54813	Unknown Human mRNA for KIAA0262 gene
326	54814	Hu.vacuolar proton pump delta polypeptide (VATD) mRNA
327	54816	Unknown Homo sapiens mRNA for KIAA0713 protein
328	54817	Unknown Hu.Chromosome 16 BAC clone CIT987SK-A- 101F10
329	54819	Homo sapiens chromokinesin KIF4 (KIF4) mRNA
330	54821	Unknown Homo sapiens cDNA FLJ11101 fis
331	54823	Human mRNA for heat shock protein hsp86
332	54824	hinge=OXPHOS system complex III mitochondrial subunit
333	54825	H.sapiens mRNA for huntingtin interacting protein HIP-I
334	54826	Homo sapiens kinesin light chain mRNA
335	54827	Homo sapiens kinesin light chain mRNA
336	54829	Novel
337	54830	Unknown complete sequence
338	54832	Unknown Homo sapiens cDNA FLJ20272 fis
339	55800	Homo sapiens mRNA for E-MAP-115/105

SEQ ID NO:	Clone ID #	Genbank Homologies
340	55801	Hu. U-snRNP-associated cyclophilin (USA-CyP) mRNA
341	55803	Human chromosome 14 DNA sequence
342	55804	Human thymosin beta-4 mRNA
343	55805	Homo sapiens huntingtin interacting protein 1 (HIP1)
344	55806	Hu. protein kinase, interferon-inducible double stranded RNA
345	55808	Homo sapiens glutathione S-transferase A4 (GSTA4) mRNA
346	55810	Human chromosome 14 DNA sequence
347	55811	Unknown Homo sapiens mRNA for KIAA0713 protein
348	55812	Novel
349	55814	Human poly(ADP-ribose) synthetase mRNA
350	55816	Novel
351	55817	Homo sapiens centromere protein E (CENPE) mRNA
352	55819	Human poly(ADP-ribose) polymerase mRNA
353	55820	Novel
354	55823	Human mRNA for heat shock protein hsp86
355	55824	Novel
356	55826	Homo sapiens SOX18 mRNA, complete cds
357	55828	Novel
358	55829	Novel
359	55831	Unknown BAC sequence from the SPG4 candidate region
360	55832	Homo sapiens heat shock transcription factor 2 (HSF2)
361	55833	Homo sapiens vacuolar H-ATPase subunit D mRNA
362	55834	Homo sapiens clone 628 unknown mRNA
363	55835	Human mRNA for Cu/Zn superoxide dismutase (SOD).
364	55838	Homo sapiens cDNA FLJ20473 fis, clone KAT07092

The expression levels of certain of the isolated antigens in lung tumor tissues compared to expression levels in 36 normal tissues was determined using microarray technology and either computer or visual analysis. The results of these studies are shown below in Table 7, together with the databank analyses for these sequences. These results indicate that these antigens are over-expressed in lung tumor tissue compared to normal tissue.

Table 7

Clone Name	SEQ ID NO:	Description	Ratio T/N Mean/Med
SCC3-5	320	Novel	visual
SCC3-7	321	=SCC3-52; Unknown FLJ20272	visual
SCC3-17	325	Ring finger protein 10	2.1/3.0 ad
SCC3-30	330	Unknown FLJ11101	visual
SCC3-52	338	Unknown cDNA FLJ20272	2.7/1.2 sm
SCC3-64	340	U-snRNP-assoc. cyclophilin	visual
SCC3-71	341	TNG-2	visual
SCC3-79	345	GST A4	visual
SCC3-87	349	Poly(ADP-ribose) synthetase	visual
SCC3-90	440	Polyadenylate binding pro (TIA-1)	visual
SCC3-111	359	Unknown BAC	visual
SCC3-112	360	Heat-shock transcription factor 2	visual

5 Ratio T/N = lung tumor tissues over normal tissues

EXAMPLE 6

ANALYSIS OF cDNA EXPRESSION USING MICROARRAY TECHNOLOGY

10 In additional studies, sequences disclosed herein were found to be overexpressed in specific tumor tissues as determined by microarray analysis. Using this approach, cDNA sequences are PCR amplified and their mRNA expression profiles in tumor and normal tissues are examined using cDNA microarray technology essentially as described (Shena *et al.*, 1995). In brief, the clones are arrayed onto glass slides as multiple replicas, with each location corresponding to a unique cDNA clone

15 (as many as 5500 clones can be arrayed on a single slide, or chip). Each chip is hybridized with a pair of cDNA probes that are fluorescence-labeled with Cy3 and Cy5, respectively. Typically, 1 μ g of polyA⁺ RNA is used to generate each cDNA probe. After hybridization, the chips are scanned and the fluorescence intensity recorded for both Cy3 and Cy5 channels. There are multiple built-in quality control steps. First, the

20 probe quality is monitored using a panel of ubiquitously expressed genes. Secondly, the control plate also can include yeast DNA fragments of which complementary RNA may be spiked into the probe synthesis for measuring the quality of the probe and the sensitivity of the analysis. Currently, the technology offers a sensitivity of 1 in 100,000

copies of mRNA. Finally, the reproducibility of this technology can be ensured by including duplicated control cDNA elements at different locations.

Clones SCC2-5 (SEQ ID NO:229), SCC2-14 (SEQ ID NO:230), SCC2-50 (SEQ ID NO:231) and SCC2-51 (SEQ ID NO:232) were found to be overexpressed by microarray analysis in adenocarcinoma, lung pleural effusion, squamous cell carcinoma, small cell carcinoma, colon tumor, and ovarian tumor, with low levels of expression being detected in all normal tissues tested. The normal tissues included in the microarray were lymph node, salivary gland, lung, bladder, bone marrow, bronchus, esophagus, kidney, heart, liver, lung, skeletal muscle, spleen, stomach, PBMC, skin, thymus, tonsil, trachea, pituitary gland, adrenal gland, brain, pancreas, thyroid gland, adult lung, colon, small intestine, ovary, and peritoneal epithelium. These cDNAs were cloned from a lung small cell carcinoma expression library using small cell carcinoma patient sera as a probe. SCC2-14 has some similarity to an RNA-binding protein, and SCC2-50 is homologous to hypoxia-inducible factor 1 alpha. Amino acid sequences encoded by these cDNAs (SEQ ID Nos:229-232) are shown in SEQ ID NOs:233-236, respectively.

Also by microarray analysis, SCC2-54 (SEQ ID NO:178) was found to be over-expressed in lung small cell and squamous carcinomas relative to normal tissues. An extended cDNA sequence for this clone is provided in SEQ ID NO:396, encoding the polypeptide sequence set forth in SEQ ID NO:397.

LSC-49 (SEQ ID NO:29) was found to be overexpressed in lung carcinomas, particularly small cell lung carcinomas. An extended sequence for this clone is provided in SEQ ID NO:412, encoding an amino acid sequence set forth in SEQ ID NO:413. Database searches of LSC-49 revealed sequence homology with a GTPase-activating protein for Rac (mgcRacGAP).

The results of an additional microarray analysis, performed using a criteria of greater than or equal to 2-fold over-expression in tumors and the average expression in normal tissues less than or equal to 0.2 (range from 0.01-10), are summarized in Table 8 below.

Table 8

Chip #	Clone ID #	Ratio	Mean Signal 1	Mean Signal 2	SEQ ID NO:
5	56908	3.78	0.837	0.221	398, 243
5	56911	2.29	0.453	0.198	399, 245
5	56912	2.57	0.265	0.103	400, 247
5	56913	2.21	0.306	0.138	401, 249
5	56916	2.44	0.449	0.184	402, 251
5	56917	2.29	0.479	0.209	403, 252
5	56921	2.54	0.418	0.165	404, 253
5	56922	5.05	0.613	0.121	405, 255
5	56923	2.74	0.426	0.155	406, 257

5 The ratio of signal 1 to signal 2 in Table 8 above provides a measure of the level of expression of the identified sequences in tumor versus normal tissues. For example, for SEQ ID NO:398, the tumor-specific signal was 3.78 times that of the signal for the normal tissues tested; for SEQ ID NO:399, the tumor-specific signal was 2.29 times that of the signal for normal tissues, etc.

10 Results from an additional microarray analysis, performed using visual analysis for identifying cDNAs over-expressed in selected tumor samples, are provided in Table 9 below. Some of these cDNAs were preferentially over-expressed in small cell lung carcinoma (SCLC) samples even though the original cDNAs were identified from subtracted NSCLC tumor samples.

Table 9

Chip #	Clone ID #	Ratio	Mean Signal 1	Mean Signal 2	SEQ ID NO:
5	60974	3.84	0.584	0.152	407
5	60976	3.73	0.58	0.155	408
5	60977	3.84	0.492	0.128	409
5	60978	4.63	0.476	0.103	410
5	60980	3.4	0.557	0.164	411

- 5 In further studies, the expression levels of certain of the isolated antigens in lung tumor tissues previously disclosed in Example 4 were compared to the expression levels in 36 normal tissues using microarray technology and computer analysis. The results of these studies are shown below in Table 10.

Table 10

Clone Name	Clone ID #	SEQ ID NO:	Squa/N	Aden/N	SC/N
LSCC2-1	54533	258	3	2	1
LSCC2-2	54534	259	5	3	5
LSCC2-4	54536	260	3	2	2
LSCC2-8	54540	262	0	3	2
LSCC2-18	55084	263	2	2	1
LSCC2-23	54555	265	2	3	3
LSCC2-25	54557	266	2	1	1
LSCC2-32	54564	267	2	3	2
LSCC2-48	55473	269	4	2	1
LSCC2-58	55104	270	3	5	2
LSCC2-61	55107	272	2	5	3
LSCC2-75	55483	277	2	4	2
LSCC2-79	55487	279	3	2	2
LSCC2-93	55089	282	5	4	4
LSCC2-121	55490	289	4	2	2
LSCC2-127	55495	290	2	4	1
LSCC2-137	55504	291	0	3	8
LSCC2-139	55506	292	3	4	1
LSCC2-161	56480	293	3	2	1
LSCC2-164	56482	294	2	4	2
LSCC2-171	56488	297	6	4	5
LSCC2-178	56494	300	3	5	3
LSCC2-191	56517	303	5	2	2

- 5 Squa/N = Squamous lung tumor over Normal tissues
 Aden/N = Adenocarcinoma over Normal tissues
 SC/N = Lung Small Cell carcinoma over Normal tissues

10

EXAMPLE 7**FURTHER CHARACTERIZATION OF THE LUNG TUMOR ANTIGEN L43E**

- The predicted protein sequence shown in SEQ ID NO:436 represents a second open reading frame (ORF-2) encoded by the SCC2-51 cDNA nucleotide sequence (also referred to as L43E). The SCC2-51 nucleotide sequence is shown in
- 15 SEQ ID NO:175. This protein sequence has 33% identity and 49% similarity to the polypeptide of the fish Takifugu rubripes retrotransposon. Motif searches indicate potential protease signatures and protein translocation analysis indicates that the protein

could be cytoplasmic or membrane-associated due to a potential transmembrane region. Using realtime PCR, SCC2-51 was found to be over-expressed in primary small cell carcinoma and in atypical carcinoid metastatic tumors, but weakly expressed in other lung carcinomas and normal tissues except for pituitary gland and adrenal gland. The
5 cDNA sequence and ORF-1 have homology to Takifugu rubripes gag polyprotein (28% identity and 45% similarity).

EXAMPLE 8

ISOLATION OF cDNA SEQUENCES FOR ADDITIONAL LUNG TUMOR ANTIGENS

10 Additional cDNA clones were obtained from analysis II of LST-S6 and Mets3616-S1 libraries of Lung Chip V. These cDNAs were differentially expressed in lung squamous and/or adenocarcinoma tumors (greater than or equal to 2 fold), and the average expression values for these clones in normal tissues were below 0.1 (the range of value was between 0.001 and 10). A total of 29 non-redundant cDNA sequences were
15 isolated and are disclosed in SEQ ID NO:367-395. A summary of these clones with respect to the Genbank searches is shown in Table 11.

Table 11

<u>SEQ ID NO:</u>	<u>Clone ID #</u>	<u>Chip #</u>	<u>GenBank</u>
367	49949	5	Novel
368	49952	5	Collagen type IV alpha-5
370	49960	5	h. mRNA for Pirin, isolate 17
371	49961	5	vector/Novel
372 and 373	49962	5	HBP, heme binding protein
374	49965	5	h. testitin
375	49966	5	KIAA 1077
376	49977	5	Cyclin B homologue
377	49975	5	Cat Eye 22q11.2
378	49982	5	Novel
379	49986	5	Novel
380	49988	5	KIAA0292, similar to AR1 protein
381	49993	5	transferrin receptor
382	49995	5	Cathepsin B
383	49996	5	RP3, similar to mouse tctex-1
384	49999	5	Novel, Cosmid g1572c198
385	50006	5	sheep and mouse sox2 gene (HMG box, germ cell)
386	50007	5	Nrf3 for NF-E2 related factor 3
387	50009	5	vector/Novel, chrom. 10 seq
388	50014	5	clone RP5-1025A1 on 20p11.21
389	50016	5	Failed/h. MEGF9
390	50017	5	NH0160k17
391	50019	5	None
392	50022	5	h mitotic kinesin-like protein-1
393	50023	5	KIAA1077
394	50024	5	None
395	50033	5	None

EXAMPLE 9

REAL-TIME PCR ANALYSIS OF L578S

5 As previously shown in Example 2, clone 48137 (SEQ ID NO:89), which is also referred to as L578S, and is predicted to have an extended cDNA sequence of SEQ ID NO:365, was shown to be 5-fold over-expressed in lung tumors as compared to the normal tissue by microarray analysis. Real-time PCR analysis confirmed that L578S is over-expressed in both lung squamous and adenocarcinoma
10 tumors. Database analysis identified two human proteins showing some degree of homology to L578S, one corresponding to a putative type Ib membrane-bound protein. Protein alignment between this protein and SEQ ID NO:365 indicated that L578S full-length protein may also be a type Ib membrane-protein. This indicates that L578S is an attractive target for the development of antibody-based therapeutics.

EXAMPLE 10

SYNTHESIS OF POLYPEPTIDES

20 Polypeptides are synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence is attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage
25 of the peptides from the solid support is carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides are precipitated in cold methyl-t-butyl-ether. The peptide pellets are then dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-
30 60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) is used to elute the peptides. Following lyophilization of the pure fractions, the peptides are

characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

5 From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

1. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440;

(b) complements of the sequences provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440;

(d) sequences that hybridize to a sequence provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440, under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440; and

(g) degenerate variants of a sequence provided in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440.

2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:229-232, 237-242, 397, 413 and 425-436;

(b) sequences encoded by a polynucleotide of claim 1; and

(c) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1; and

(d) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1.

3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

4. A host cell transformed or transfected with an expression vector according to claim 3.

5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.

6. A method for detecting the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;
- (c) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

7. A fusion protein comprising at least one polypeptide according to claim 2.

8. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO:1-232, 243-396, 398-412, 414-424 and 437-440 under moderately stringent conditions.

9. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 1,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

10. An isolated T cell population, comprising T cells prepared according to the method of claim 9.

11.. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1;
- (c) antibodies according to claim 5;
- (d) fusion proteins according to claim 7;
- (e) T cell populations according to claim 10; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.

12. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 11.

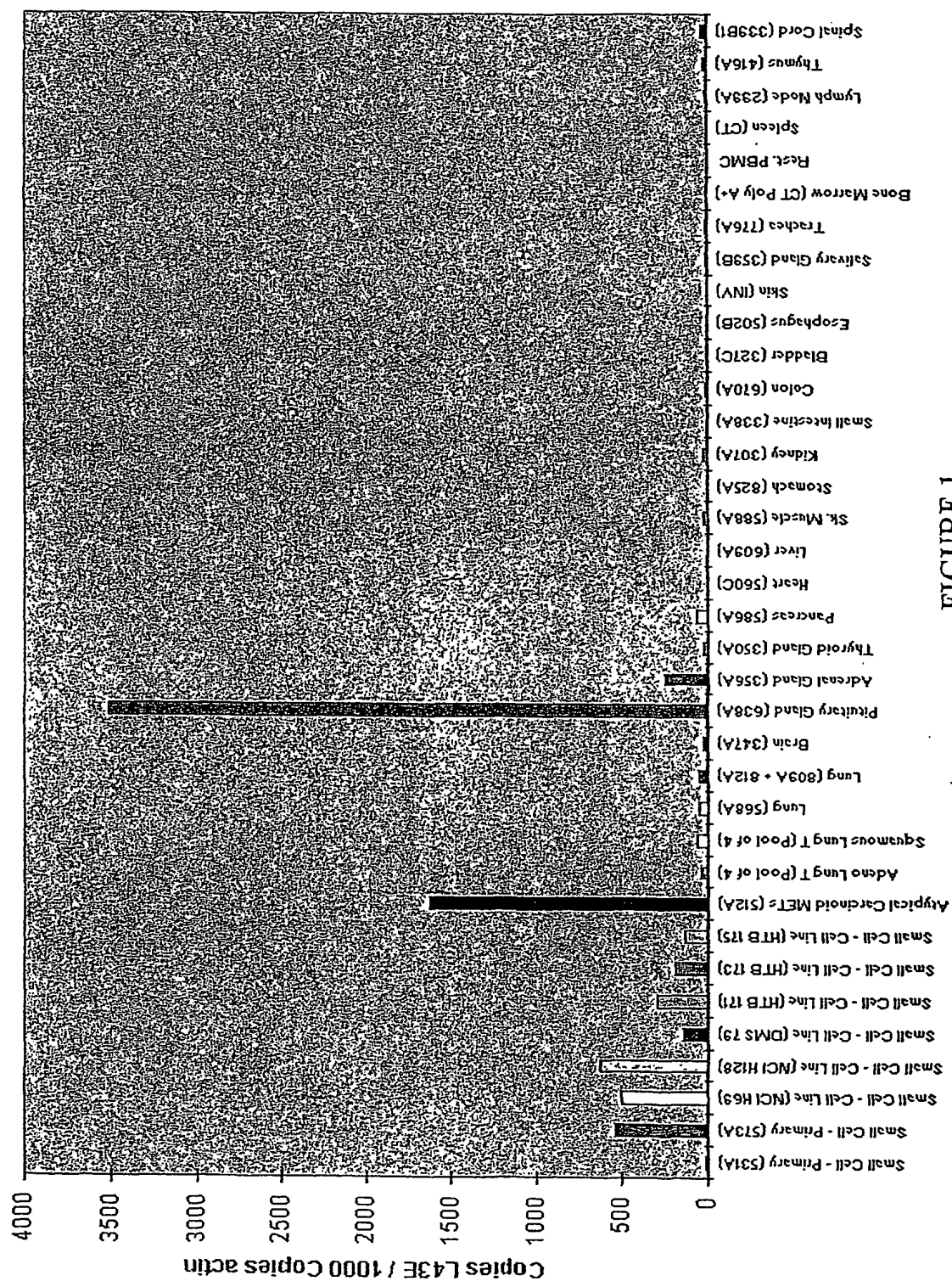
13. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 8;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

14. A diagnostic kit comprising at least one oligonucleotide according to claim 8.

15. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.

L43E: SCC2-51



SEQUENCE LISTING

<110> Corixa Corporation
 Lodes, Michael J.
 Wang, Tongtong
 Mohamath, Raodoh
 Indirias, Carol Y.

<120> COMPOSITIONS AND METHODS FOR THE THERAPY
 AND DIAGNOSIS OF LUNG CANCER

<130> 210121.512PC

<140> PCT

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gtcacagggc	accgctggct	gaaggggggc	gtgggtgctga	aggaggacgc	gctgcccggc	240
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ctccccgagc	ccatgggcac	ggccaacatc	cagctccacg	ggcctccan	agtgaaggt	360
tgtgaagtgc	tcaagaacac	atcaacgagg	gggagacggc	catgctggtc	tgcaagtcag	420
agtcctgtgc	acctgtgcac	ttgactgggc	ctggtacaaa	gatcacttga	cttttgaagg	480
acaaggccct	tattgaaccg	gcttcc				506

<210> 16
 <211> 286
 <212> DNA
 <213> Homo sapien

gaattcggca	cgagctttta	aggagaaaat	gtgacacttg	tgaaaaagct	tgtaagaaag	60
cccctccctt	ttttctttta	acctttaaat	gacaaatcta	ggtaattaag	gttgtgaatt	120
tttatctttg	ctttgttttt	aatgaacatt	tgtctttcag	aataggattg	tgtgataatg	180
tttaaatggc	aaaaacaaaa	catgattttg	tgcaattaac	aaagctactg	caagaaaaat	240
aaaacacttc	ttggtaacac	aaaaaaaaaa	aaaaaaaaaa	ctcgag		286

<210> 17
 <211> 387
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature

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<222> (1)...(387)

<223> n = A,T,C or G

<400> 17

gaattcggca	cnaggcaagg	tgtgcgggcg	ggaaggggca	cgggcacccc	cgcggtcccc	60
gggaggctag	agatcatgga	agggaagtgg	ttgctgtgta	tggttactgg	gcttgggaact	120
gctattgttg	aggctcatga	tggacatgat	gatgatgtga	ttgatattga	ggatgacctt	180
gacgatgtca	ttgaagaggt	agaagactca	aaaccagata	ccactgctcc	tccttcacat	240
cccaagggtta	cttacaaagc	tccagttcca	acaggggaag	tatatattgc	tgattctttt	300
gacagaggaa	ctctgtcagg	gtggatttta	tccaaagcca	agaaagacna	tcccgatgat	360
gaaattgcc	aatatgatgg	aaagtgg				387

<210> 18

<211> 415

<212> DNA

<213> Homo sapien

<400> 18

gaattcggca	cgagccaaag	tgagcagtag	ccaacatgtc	aggggtgggag	tcattattaca	60
aaaccgaggg	cgatgaagaa	gcagaggaag	aacaagaaga	gaaccttgaa	gcaagtggag	120
actataaata	ttcaggaaga	gatagtttga	tttttttggt	tgatgcctcc	aaggctatgt	180
ttgaatctca	gagtgaagat	gagttgacac	cttttgacat	gagcatccag	tgtatccaaa	240
gtgtgtacat	cagtaagatc	ataagcagtg	atogagatct	cttggctgtg	gtgttctatg	300
gtacccgaga	aagacaaaaa	ttcagtgaat	tttaaaaata	tttacgtctt	acaggagctg	360
gataatccag	gtgcaaaacg	aattctagac	tttgccagtt	taaggggcag	caggg	415

<210> 19

<211> 466

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(466)

<223> n = A,T,C or G

<400> 19

gaattcggca	cnagcgggga	tcggctgcct	gagaggtatc	acctcttctg	ggctcaagat	60
ggacaacaag	aagcgcctgg	cctacgccat	catccagttc	ctgcatgacc	agctccggca	120
cgggggcttc	tcgtccgatg	ctcaggagag	cttggaaagc	gccatccagt	gcctggagac	180
tgcgtttggg	gtgacggtag	aagacagtga	ccttgcgctc	cctcagactc	tgccggagat	240
atgtgaagcg	gctgccacgg	gcaaggagat	gccgcaggac	ctgaggagcc	ccgcgcgaac	300
cccgcccttc	cgaagaagga	ctcancaaga	agggcaagaa	gccgccttca	aaacccgaaa	360
gggaaaaccg	aagccagaat	gaaaaagtgg	gaaaaacttt	tgaaagcttg	cccgtgccat	420
ttttcttacc	gggaaaaaag	cccattcgga	agcttcaaac	cccaa		466

<210> 20

<211> 296

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(296)

<223> n = A,T,C or G

<400> 20

gaattcggca	cnagggtggtg	tgtggctgcg	gcctgggcaa	gagccgccgc	ggaccatgag	60
ctgagtaagt	tctggaggga	tcctgcctct	tggagccttc	gcagccaggc	agctgtgaac	120

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tgtgagctag	agtgaagcag	aaatctagga	agatgagctc	caagatggtc	ataagtgaac	180
caggactgaa	ttgggatatt	tcccccaaaa	atggccttaa	gacatttttc	tctcagaaaa	240
ttataaagat	cattccatgg	cttccaagtt	taaaaagaac	ttacgtgggt	tttatc	296

<210> 21
 <211> 328
 <212> DNA
 <213> Homo sapien

<400> 21						
gaattcggca	cgagcccgcg	ctgcacttgc	tgcgcgcgtg	actggaggac	cgagccccc	60
cattttcttt	atgtggttgt	ggtgggggca	cagtaatgcc	ctgtgcgcgc	tagcgttcct	120
gtgggggatgt	ggccgggggg	cgtcgggaag	cgtcactgct	tgatgtccga	gctcagcgat	180
gaagccagcg	agccgggaact	cctgaaccgc	agcttgtcca	tgtggcacgg	gctcgggaca	240
caggtcagcg	gggaggagct	ggatgtcccc	ctggatcttc	acacagctgc	ttcattggcc	300
agtatgaagt	ggtgaaggaa	tgtgtgca				328

<210> 22
 <211> 466
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(466)
 <223> n = A,T,C or G

<400> 22						
gaattcggca	cgaggcggac	taataaaggc	catggcgcca	gcagaaatcc	tgaacgggaa	60
ggagatctcc	gcgcaaataa	ggcgagact	gaaaaatcaa	gtcactcagt	tgaaggagca	120
agtacctggt	ttcacaccac	gcctggcaat	attacaggtt	ggcaacagag	atgattccaa	180
tctttatata	aatgtgaagc	tgaaggctgc	tgaagagatt	gggatcaaag	ccactcacat	240
taagttacca	agaacaacca	cagaatctga	ggtgatgaag	tacattacat	ctttgaatga	300
agactctact	gtacatgggt	tcttagtgca	gctaccttta	gattcagaga	attccattaa	360
cactgaagaa	gtgatcaatg	ctattgcacc	cganaaggat	gtggatggat	tgactagcat	420
caatgctggg	aaacttgcta	gaggtgacct	caatgactgt	ttcatt		466

<210> 23
 <211> 517
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(517)
 <223> n = A,T,C or G

<400> 23						
gaattcggca	cgagcagagg	tctccagagc	cttctctctc	ctgtgcaaaa	tggcaactct	60
taaggaaaaa	ctcattgcac	cagttgcgga	agaagaggca	acagttccaa	acaataagat	120
cactgtagt	ggtgttgac	aagttggtat	ggcgtgtgct	atcagcattc	tgggaaagtc	180
tctggctgat	gaacttgctc	ttgtggatgt	tttgggaagat	aagcttaaag	gagaaatgat	240
ggatctgcag	catgggagct	tatttcttca	gacacctaaa	attgtggcag	ataaagatta	300
ttctgtgacc	gccaattcta	agattgtagt	ggtaactgca	ggagtccgtc	agcaagaagg	360
ggagagtcgg	ctcaatctgg	tgcaagagaaa	tgtaaatgtc	ttcaaattca	ttattcctca	420
gatcgtcaag	tacagtcctg	attgcatcat	aattgtggnt	tccaaccag	tggacattct	480
tacgtatggt	acctggaaac	taagtggatt	acccaaa			517

<210> 24

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<211> 196
 <212> DNA
 <213> Homo sapien

<400> 24
 gaattcggca cgagggtggc actatgtggc gcgctctgtc ggcacgggct cagaatgtag 60
 ccccatgggc gggactcgag gctcgggtga cggccttgca ggaggtagcc ggaactccac 120
 gagtgacctc gcatctggc ccggctcccg ctgctcgcaa cagcgtgact acagggtatg 180
 gcgggggtccg ggcact 196

<210> 25
 <211> 365
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(365)
 <223> n = A,T,C or G

<400> 25
 gaattcggca cgagggtggg cgggtgctggt ttttcgctcg tcgactgcgg ctcttcctcg 60
 ggcagcggaa gcggcgcggc ggtcggagaa gtggcctaaa acttcggcgt tgggtgaaag 120
 aaaatggccc gaaccaagca gactgctcgt aagtccaccg gtgggaaagc cccccgcaaa 180
 cagctggcca cgaaagccgc caggaaaaagc gctccctcta cggcgggggg gaagaagcct 240
 catcgctaca ggcccgggac cgtggcgctt cganagattc gtcgttatca gaagtcgacc 300
 gagctgctca tccggaagct gcccttccag angttgggtga gggagatcgc gcaggatttc 360
 aaac 365

<210> 26
 <211> 321
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(321)
 <223> n = A,T,C or G

<400> 26
 ctcgagtttt tttttttttt tttttttgta cgaaatggct aagttttattc aacatctcgg 60
 atattcatct ggatattggg tttgttttgt gatacaatac atattcacct taactggtgc 120
 tactgcaaag aaagctttct tgacctgcat gacgtgcctc anagcttctc tccaccaatt 180
 ggaaccaccc aaagcctagt ctanaccaa gtgctctgga gaaaaaaaaac aaaacaaaaa 240
 aacagcaaac agaaaacagt tgtgccccca aaagtactca gaagtcatat gttattttaca 300
 attggggttg tgtgggatgg g 321

<210> 27
 <211> 454
 <212> DNA
 <213> Homo sapien

<400> 27
 gaattcggca cgagcaagga tgaggagaac aatccccttg agacagaata tggcctttct 60
 gtctacaagg atcaccagac catcaccatc caggagatgc cggagaaggc cccagccggc 120
 cagctccccc gctctgtgga cgtcattctg gatgatgact tgggtggataa agcgaagcct 180
 ggtgaccggg ttcagggtgg gggaaacctac cgttgccctc ctggaaagaa gggaggctac 240
 acctctggga ccttcaggac tgtcctgatt gcctgtaatg ttaagcagat gagcaaagga 300
 tgctcagccc tctttctctg ctgaggatat agccaagatc aagaagttca gtaaaacccg 360

9

atccaaggat	atctttgacc	atctggccaa	gtcattggcc	ccaagtatcc	atgggcatga	420
ctatgtcaag	aaagcaatcc	tctgcttgct	cttg			454

<210> 28
 <211> 285
 <212> DNA
 <213> Homo sapien

<400> 28						
gaattcggca	cgagggttgg	ctgaaattca	tgcaagcttc	cgaagatctt	ctcaaggaac	60
actacgttga	cctgaaggac	cgtccattct	ttgccggcct	ggtgaaatac	atgcactcag	120
ggccggtagt	tgccatggtc	tgaggagggc	tgaatgtgg	gaaaacgggc	cgagtcatgc	180
tcggggagac	caaccctgca	gactccaagc	ctgggaccat	ccgtggagac	ttctgcatac	240
aagttggcag	gaacattata	catggcagtg	attctgtgga	gagtg		285

<210> 29
 <211> 512
 <212> DNA
 <213> Homo sapien

<400> 29						
gaattcggca	cgagcaacct	tgtaaattgt	aaagtacaac	tcgtatttat	ctctgatgtg	60
ccgctggctg	aactttgggt	tcatttgggg	tcaaagccag	tttttctttt	aaaattgaat	120
tcattctgat	gcttggcccc	cataccccca	accttgtcca	gtggagccca	acttctaaag	180
gtcaatata	catcctttgg	catcccaact	aacaataaag	agtaggctat	aagggaagat	240
tgtcaatatt	ttgtggtaag	aaaagctaca	gtcatttttt	ctttgcactt	tggtatgctga	300
aatttttccc	atggaacata	gccacatcta	gatagatgtg	agctttttct	tctgttaaaa	360
ttattcttaa	tgtctgtaaa	aacgattttc	ttctgtagaa	tgtttgactt	cgtattgacc	420
cttatctgta	aaacacctat	ttgggataat	atttggaata	aaagtaaata	gctttttcaa	480
aatgaaaaaa	aaaaaaaaaa	aaaaaactcg	ag			512

<210> 30
 <211> 464
 <212> DNA
 <213> Homo sapien

<400> 30						
gaattcggca	cgaggccagg	tgggcagccc	gcggaaccgac	ccctactcgg	cgggcgcaact	60
ccacaaccag	tacggcccca	tgaatatgaa	catgggtatg	aacatggcag	cagccgcggc	120
ccaccaccac	caccaccacc	accaccaccc	cggtgccttt	ttcccgctat	atgcggcagc	180
agtgcatcaa	gcaggagcta	atctgcaagt	ggatcgaccc	cgagcaactg	agcaatccca	240
agaagagctg	caacaaaact	ttcagcacca	tgacagagct	ggtgacacac	gtctcgggtg	300
agcacgtcgg	cggcccggag	cagagcaacc	acgtctgctt	ctgggaggag	tgtccgcgcg	360
agggcaagcc	cttcaaggcc	aaatacaaac	tggtcaacca	catccgcgtg	cacacaggcg	420
agaaaccctt	cccctgcccc	ttcccggtg	gtggcaaatg	cttc		464

<210> 31
 <211> 317
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(317)
 <223> n = A,T,C or G

<400> 31						
gaattcggca	cgagcagagg	tgagcaagct	ggaacagcaa	tgccagaagc	agcaggagca	60
ggctgacagc	ctggaacgca	gcctcgaggc	tgagcgggcc	tcccggtg	agcgggacag	120

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tgctctggag	actctgcagg	gccagttaga	ggagaaggcc	cangagctag	ggcacagtca	180
gagtgcccta	gcctcggccc	aacgggagtt	ggctgccttc	cgcaccaagg	tacaagacca	240
cagcaaggct	gaagatgagt	ggaaggccca	gttggcccgg	ggccggcaag	aggctganag	300
gaaaaatagc	ctcatca					317

<210> 32
 <211> 275
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(275)
 <223> n = A,T,C or G

<400> 32						
gaattcggca	cgagcgaagg	aggacggagg	cttcagacac	tcggaagcct	ttgaggcact	60
ccagcaaaaag	agtcaggagac	tggaactccag	gctccagcac	gtggaggatg	gggtgctctc	120
catgcagggtg	gcttctgcgc	gccagaccga	gagcctggag	tccctcctgt	ncaagagcca	180
ggagcacgag	cagcgcctgg	ccgccctgca	ggggcgccctg	gaaggcctcg	ggtcctcata	240
ggcanaccan	gatggcctgc	cagcacggtg	aggag			275

<210> 33
 <211> 516
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(516)
 <223> n = A,T,C or G

<400> 33						
gaattcggca	cgagggggcc	tgggcgttga	ctgtgggaaa	ctcggaaca	agctcacatc	60
ttcctgtggg	aaaccttcta	gcaacaggat	gagtcctgcag	tggaactgcag	ttgccacctt	120
cctctatgcg	gaggtcctttg	ttgtgttgct	tctctgcatt	tccttcattt	ctcctaaaag	180
atggcagaag	attttcaagt	cccggctggg	ggagttgtta	gtgtcctatg	gcaacacctt	240
ctttgtggtt	ctcattgtca	tccttgtgct	gttggtcac	gatgccgtgc	gcgaaattcg	300
gaagtatgat	gatgtgacgg	aaaagggtgaa	cctccagaac	aatcccgggg	ccatggagca	360
cttccacatg	aagnttttcc	gtgccagag	gaatctctac	attgctggct	tttcccttgc	420
gctgtccttc	ctgcttagac	gcctgggtgac	tctcatttcc	aacaggccac	gctgctggcc	480
ttcaatgaac	ctttaaaaac	aggcggagag	tnctat			516

<210> 34
 <211> 446
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(446)
 <223> n = A,T,C or G

<400> 34						
gaattcggca	cgagacagaa	atgnctaaag	aagagaagga	ccctggaatg	ggtgcaatgg	60
gtggaatggg	agggtggtatg	ggagggtggca	tggttctaact	cctagactag	tgctttacct	120
ttattaatga	actgtgacag	gaagcccaag	gcagtgttcc	tccaataaac	ttcagagaag	180
tcanttgag	aaaatgaaga	aaaaggctgg	ctgaaaatca	ctataaccat	cagttactgg	240
tttcagttga	caaaatatat	aatggtttac	tgctgtcatt	gtccatgcct	acagataatt	300

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tat	ttt	gaataa	aaaacatttg	tacattcctg	atactgggta	caagagccat	360
gtaccagtgt	actgctttca	acttaaataca	ctgaggcatt	tttactacta	ttctgttaaa		420
atcaggattt	tagtgcttgc	ccccca					446

<210> 35

<211> 440

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(440)

<223> n = A,T,C or G

<400> 35

gaattcggca	cgaggtttat	ttgtccccac	cagaaggttg	gggtgggagg	gcctagaaca	60
cagcgtgcgg	cgggttcccg	ggtggagcca	gcgcagacag	cgtgggtccc	tgcggtctct	120
angcgaaggt	ggagttgttc	cancccacat	tggcccgctg	ttcattgtcg	taatagttga	180
tgtagaccct	gtccgggctg	atgcgcaggc	gctctgccag	caggccgcac	agcagcttgc	240
tgtaggagcg	gttctgcgcg	ccgccgatct	tgccgatgct	gtgcangctg	canagcgcg	300
acggctcgct	ggagccgccc	aaggccatga	gctggtccgg	gaccacgtgc	accgctatgt	360
actggggggg	cttgccgggtg	gcctgcgcca	nctgctgggt	gagctcggag	aggaaccgtc	420
cggcacggag	gcgcggggca					440

<210> 36

<211> 373

<212> DNA

<213> Homo sapien

<400> 36

gaattcggca	cgaggccaaa	cgtaccaaga	aagtcgggat	cgtcggtaaa	tacgggaccc	60
gctatggggc	ctccctcccg	aaaatggtga	agaaaattga	aatcagccag	cacgccaagt	120
acacttgctc	tttctgtggc	aaaaccaaga	tgaagagacg	agctgtgggg	atctggcact	180
gtggttcctg	catgaagaca	gtggctggcg	gtgcctggac	gtacaatacc	acttccgctg	240
tcacggtaaa	gtccgcctatc	agaagactga	aggagttgaa	agaccagtag	acgctcctct	300
actctttgag	acatcactgg	cctataataa	atgggttaat	ttatgtaaca	aaaaaaaaaa	360
aaaaaaactc	gag					373

<210> 37

<211> 565

<212> DNA

<213> Homo sapien

<400> 37

gaattcggca	cgaggggggca	cgggcacccc	cgcggtcccc	gggaggctag	agatcatgga	60
agggaaagtgg	ttgctgtgta	tggtactggg	gcttggaact	gctattgttg	aggctcatga	120
tggacatgat	gatgatgtga	ttgatattga	ggatgacctt	gacgatgtca	ttgaagaggt	180
agaagactca	aaaccagata	ccactgctcc	tccttcatct	cccaaggtta	cttacaaagc	240
tccagttcca	acaggggaag	tatatatttg	tgattctttt	gacagaggaa	ctctgtcagg	300
gtggatttta	tccaaagcca	agaaagacga	taccgatgat	gaaattgcca	aatatgatgg	360
aaagtgggag	gtagaggaaa	tgaaggagtc	aaagcttcca	ggtgataaag	gacttgtgtt	420
gatgtctcgg	gccaaagcatc	atgccatctc	tgctaaactg	aacaagccct	tcctgtttga	480
caccaagcct	ctcttggttca	gtatgagggtt	aatttcctaaa	atggaataga	atgtggtggt	540
gcctatgtga	aactgctttc	taaaa				565

<210> 38

<211> 566

<212> DNA

<213> Homo sapien

12

<220>

<221> misc_feature

<222> (1)...(566)

<223> n = A,T,C or G

<400> 38

gaattcggca	cgagcccaac	tttagccagg	aagatcagca	ggacacccag	atttatgaga	60
agcatgacaa	ccttctacat	gggaccaaga	agaaaaagga	gaagatggtg	agtgcagcat	120
tcatgaagaa	gtacatccat	gtggccaaaa	tcatcaagcc	tgtcctgaca	caggagtcgg	180
ccacctacat	tgcagaagag	tattcacgcc	tgcgcagcca	ggatagcatg	agctcagaca	240
ccgccaggac	atctccagtt	acagcccga	cactggaaac	tctgattcga	ctggccacag	300
cccatgcgaa	ggcccgcag	agcaagactg	tggacctgca	ggatgcagag	gaagctgtgg	360
agttggtcca	gtatgcttac	tttaagaagg	ttctggagaa	ggagaagaaa	cgtaagaagc	420
gaagtgagga	tgaatcagag	acagaagatg	aagaggagaa	aagccaagag	gaccaggagc	480
agaagaggaa	gagaaggga	actcgccagc	cagatgccaa	agatggggat	tcatacgacc	540
cctatgactt	cagtgcacac	gaggan				566

<210> 39

<211> 364

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(364)

<223> n = A,T,C or G

<400> 39

gaattcggca	cgaggtctca	cagaaagttc	tccgctccca	gacatgggtc	cctcggtctc	60
ctgcctcgga	agcgagcag	caggcatcgt	gggaaggtga	agagcttccc	taaggatgac	120
ccgtccaagc	cggtccacct	cacagccttc	ctgggataca	aggctggcat	gactcacatc	180
gtgcgggaag	tcgacaggcc	gggatccaag	gtgaacaaga	aggaggtggt	ggaggctgtg	240
accattgtag	agacaccacc	catggtggtt	gtgggcattg	tgggctacgt	ggaaaccctt	300
ngaggcctcc	ggaccttta	gactgtcttt	gcttgagcac	atcantgatg	aatgcaagag	360
gcgt						364

<210> 40

<211> 336

<212> DNA

<213> Homo sapien

<400> 40

gaattcggca	cgagcccaga	tctcctaccc	agcctcccag	ggggcctact	acatccctgg	60
acagggggcgt	tccacatacg	ttgtcccagc	acagcagtac	cctgtgcagc	caggagcccc	120
aggcttctat	ccaggtgcaa	gccctacaga	atttgggacc	tacgctggcg	cctactatcc	180
agcccaaggg	gtgcagcagt	ttcccactgg	cgtggccccc	gccccagttt	tgatgaacca	240
gccaccccag	attgctccca	agagggagcg	taagacgata	cgaattcgag	atccaaacca	300
aggaggaaag	gatatacacg	aggagatcat	gtctgg			336

<210> 41

<211> 566

<212> DNA

<213> Homo sapien

<400> 41

gaattcggca	cgagacttgg	gaaaatgaat	tcagaggagg	aagatgaagt	gtggcaggtg	60
atcataggag	ccagagctga	gatgacttca	aaacaccaag	agtacttgaa	gctggaaacc	120
acttggtatga	ctgcagttgg	tcttttcagag	atggcagcag	aagctgcata	tcaaactggc	180

13

gcagatcagg	cctctataac	cgccaggaat	cacattcagc	tgggtgaaact	gcaggtggaa	240
gaggtgcacc	agctctcccg	gaaagcagaa	accaagctgg	cagaagcaca	gatagaagag	300
ctccgtcaga	aaacacagga	ggaaggggag	gagcgggctg	agtcggagca	ggaggcctac	360
ctgcgtgagg	attgagggcc	tgagcacact	gccctgtctc	cccactcagt	ggggaaagca	420
ggggcagatg	ccaccctgcc	caggggttggc	atgactgtct	gtgcaccgag	aagaggcggc	480
aggtcctgcc	ctgccaatca	ggcgagacgc	ctttgtgagc	tgtgagtgcc	tcctgtggtc	540
tcaggcttgc	gcttggacct	ggttct				566

<210> 42
 <211> 386
 <212> DNA
 <213> Homo sapien

gaattcggca	cgagggcagc	tcgagtcac	cagcagcgcc	gtccgcttga	ccgagatgct	60
gcgggcctgt	cagttatcgg	gtgtgaccgc	cgccgccag	agttgtctct	gtgggaagtt	120
tgctctccgt	ccattgcgac	catgccgcag	atactctact	tcaggcagct	ctgggttgac	180
tactggcaaa	attgctggag	ctggcctttt	gtttgttggg	ggaggtattg	gtggcactat	240
cctatatgcc	aaatgggatt	cccatttccg	ggaaagtgt	gagaaaacca	taccttactc	300
agacaaactc	ttcgagatgg	ttcttggtcc	tgcagcttat	aatgttccat	tgccaaagaa	360
atcgattcaa	gtcgggtcca	ctaaaa				386

<210> 43
 <211> 514
 <212> DNA
 <213> Homo sapien

gaattcggca	cgagggcaaa	acctccacct	cctgatgaat	ttcttgactg	tttccaaaag	60
tttaaacacg	gatttaacct	tctggccaaa	ctgaagtctc	atattcagaa	tcctagtgtc	120
gcagatttgg	ttcacttttt	gtttactcca	ttaaataatg	tggtgcaggc	aacaggaggt	180
cctgaactag	ccagttcagt	acttagtccc	ctattgaata	aggacacaat	tgatttctta	240
aattatactg	tcaatgggtga	tgaacggcag	ctgtggatgt	cattggggagg	aacttggatg	300
aaagccagag	cagagtggcc	aaaagaacag	tttattccac	catatgttcc	acgattccgc	360
aatggctggg	agccccaat	gctgaacttt	atgggagcca	caatggaaca	agatctttat	420
caactggcag	aatctgtggc	aaatgtagca	gaacatcagc	gcaaacagga	aataaaaaaga	480
ttatcccaga	gcatttcagt	gtatcagaat	atta			514

<210> 44
 <211> 467
 <212> DNA
 <213> Homo sapien

gaattcggca	cgagactaga	gccgcacac	atggggactt	ctgcaaatac	agagactcgg	60
attaaagggtg	gagaagatgg	agctaaagga	actgcttatt	taatacattt	gaacaacttt	120
tggggctactt	agaagggtgct	ttgaaacctg	catttgatta	agcaagaatt	cgcttgcaag	180
ttaaaggggca	ctccacagaa	ggatgttatt	atcaagtcag	atgcaccgga	cactttgtta	240
ttggagaaaac	atgcagatta	tatgcacatc	tatgggtcaa	agaaagatga	ttatgaatac	300
tgtatgtctg	agtattttgag	aatgagtggc	atctattggg	gtctgacagt	aatggatctc	360
atgggacaac	ttcatcgcat	gaatagagaa	gagattctgg	catttattaa	gtcttgccaa	420
catgaatgtg	gtggaataag	tgctagtatc	ggacatgatc	ctcatct		467

<210> 45
 <211> 344
 <212> DNA
 <213> Homo sapien

<220>

14

<221> misc_feature
 <222> (1)...(344)
 <223> n = A,T,C or G

<400> 45
 gaattcggca cgagggagac tggaggaaga gctccgccag ctgaagtccg attcccacgg 60
 gccgaaggag tacggaggct tcagacactc ggaagccttt gaggcactcc agcaaaagag 120
 tcagggactg gactccaggc tccagcacgt ggaggatggg gtgctctcca tgcaagtggc 180
 ttctgcgcgc cagaccgaga gcctggagtc cctcctgtcc aagaaccagg aacacgagca 240
 gcgcctggcc gcctgcaggg gcgcctggaa agcctcgggt cctcagaagc agaccangat 300
 ggctgcccag cacngtgagg agcctgggag agaccagct ggtg 344

<210> 46
 <211> 303
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(303)
 <223> n = A,T,C or G

<400> 46
 gaattcggca cgagnngggaa cacaagtatg tgccaccaca ccttggtaac ttttaaattg 60
 tttttagata tgaggtctga ccatgttgcc catgccatta ttattccttt tgataaagggt 120
 gaatttaggc taaactgtga aagaatgtac agcaaatggc tctgttaatt cttctcatag 180
 gaggacagggt tactgttaat agagaacata tgtatgtaat ggctaaaaat agggcagtag 240
 aaaaggaatg taactttctca cctcctttga gaatgnaag aaagaaagaa aaaaggatgg 300
 tac 303

<210> 47
 <211> 364
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(364)
 <223> n = A,T,C or G

<400> 47
 gaattcggca cgaganatag ttccctttctc taaagtggat gaggaacaaa tgaaatataa 60
 atcggagggg aagtgtctct ctgttttggg attttgtaaa tcttctcagg ttcagagaag 120
 attcttcatg ggaaatcaag ttctaaagggt ctttgcagca agagatgatg aggcagctgc 180
 agttgcactt tccctccctga ttcatgcttt ggatgactta gacatggtgg ccatagttcg 240
 atatgcttat gacaaaagag ctaatcctca agtcggcgtg gcttttctc atatcaagca 300
 taactatgag tgtttagtgt atgtgcagct gcctttcatg gaagacttgc ggcaatacat 360
 gttt 364

<210> 48
 <211> 284
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(284)
 <223> n = A,T,C or G

15

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<400> 48
gaattcggca cgagagcagc tggaggcact ggagaaggag aaggctgcc aagctggagat      60
tctgcagcag caacttcagg tggctaataa agcccgggac agtgcccaga cctcagtgac      120
acaggccagc cgggagaagg cagagctgag ccggaagggtg gaggaactcc aggcctgtgt      180
tgagacagcc cgccaggaac agcatgaggc ccaggcccag gttgcagagc tagagttgca      240
gctgcggtct gagcagcaaa aagcaactga ganagaaagg gtgg                        284

```

```

<210> 49
<211> 313
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(313)
<223> n = A,T,C or G

```

```

<400> 49
gaattcggca cgagggtttat tatagctcat acctgggacc gattaagggtg tcaacatttt      60
aaaattactc aagatatttaa ccagaaaaga tgattatggc ctttaaaact attggacaaa      120
ctgatgctat ttaacattgt tcacagccat ttaatttgaa taacaaattt tagattctaa      180
gtaggccata acttctttgc aaaacaattg atttataaag gtacagtttc agaaggnaac      240
agcatgagac tagtcttcct ataggcacat tttagtagac tgctcttctc atccctggtc      300
aaggagcttc tct                        313

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<210> 50
<211> 522
<212> DNA
<213> Homo sapien

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```

<400> 50
gaattcggca cgagggacag ccaacaaaag cagcttcttg aagttcaact tcagcaaaat      60
aaggagctgg aaaataaata tgctaaatta gaagaaaagc tgaaggaatc tgaggaagca      120
aatgaggatc tgcgagggtc ctttaatgcc ctacaagaag agaaacaaga tttatctaaa      180
gagattgaga gtttgaaagt atctatatcc cagctaaca gacaagtaac agccttgcaa      240
gaagaaggta ctttaggact ctatcatgcc cagttaaaag taaaagaaga agaggtacac      300
agggttaagt ctttgttttc ctccctctca aagagaattg cagaactgga agaagaattg      360
gtttgtgttc aaaaggaagc tgccaagaag gtaggtgaaa ttgaagataa actgaagaaa      420
gaattaaagc atcttcacat tgatgcaggg ataatgagaa atgaaactga aacagcagaa      480
gagagagtgg cagagctagc aagagatttg gtggagatgg aa                        522

```

```

<210> 51
<211> 463
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

```

```

<400> 51
gaattcggca cgaggagcac ttcgggtcct cgcgcgctcg cgtcccctcg tgcgggctcc      60
agccgcagcc ttagcttcgg ctcccgggtt ggggtggcgcg gccgtgccct cgttttggcc      120
tccgaacgcg gctcgaatgg caagccaaaa ttcttccgg atagaatatg atacctttgg      180
tgaactaaag gtgccaaatg ataagtatta tggcgccag accgtgagat ctacgatgaa      240
ctttaagatt ggaggtgtga cagaacgcac gccaacccca gttattaaag cttttggcat      300
cttgaagcga gcggccgctg aagtaaacca ggattatggt cttgatccaa agattgctan      360
tgcaataatg aaggcagcag angaggtagc tgaaggtaaa ttaaataatc attttcctct      420

```

16

cgtgggtatgg cagactggat caggaactca gacaaatatg aat

463

<210> 52

<211> 423

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(423)

<223> n = A,T,C or G

<400> 52

gaattcggca	cgagaaagcg	cagccgagcc	cagcgccccg	cacttttctg	agcagacgtc	60
cagagcagag	tcagccagca	tgaccgagcg	ccgcgtcccc	ttctcgctcc	tgcgggggccc	120
cagctggggac	cccttcogcg	actggtaccc	gcatagccgc	ctcttcgacc	aggccttcgg	180
gctgccccgg	ctgcgggagg	agtggtcgca	gtggttaggc	ggcagcagct	ggccaggcta	240
cgtgcgcccc	ctgccccccg	ccgccatcga	gagccccgca	gtggccgcgc	ccgcctacag	300
ccgcgcgctc	agccggcaac	tcagcagcgg	ggtctcggag	atccggcaca	ctgcggaccg	360
ctggcgcgctg	tccctggatg	tcaaccactt	cgccccggac	gagctgacgg	tcaagaccaa	420
nga						423

<210> 53

<211> 474

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(474)

<223> n = A,T,C or G

<400> 53

gaattcggca	cgagggaatc	tctacattgc	tggtttttcc	ttgctgctgt	ccttcctgct	60
tagacgcctg	gtgactctca	tttcgcagca	ggccaogctg	ctggcctcca	atgaagcctt	120
taaaaagcag	gcggagagtg	ctagtgaggg	ggccaagang	tacatggagg	agaatgacca	180
gctcaagaan	ggagctgctg	ttgacggagg	caagttggat	gtcgggaatg	ctgaggtgaa	240
gttgaggagg	gagaacagga	gcctgaaggc	tgacctgcag	aagctaaagg	acgagctggc	300
cagcactaag	caaaaactag	agaaagctga	aaaccagggt	ctggccatgc	ggaagcagtc	360
tgagggcctc	accaaggagt	acgaccgctt	gctggaggag	cacgcaaagc	tgaggctgc	420
agtagatggt	cccatggaca	agaaggaaga	gtaagggcct	tccttcctcc	cctg	474

<210> 54

<211> 473

<212> DNA

<213> Homo sapien

<400> 54

gaattcggca	cgagctcgtg	ccgaatcggc	acgagggatc	ggtcgcctga	gaggtatcac	60
ctctttctggg	ctcaagatgg	acaacaagaa	gcgcctggcc	tacgccatca	tccagttcct	120
gcatgaccag	ctccggcacg	ggggcctctc	gtccgatgct	caggagagct	tggaagtgc	180
catccagtgc	ctggagactg	cgtttggggt	gacggtagaa	gacagtgacc	ttgogctccc	240
tcagactctg	ccggagatat	ttgaagcggc	tgccacgggc	aaggagatgc	cgcaggacct	300
gaggagccca	gcgcgaaccc	cgccttcoga	ggaggactca	gcagaggcag	agcgcctcaa	360
aaccgaagga	aacgagcaga	tgaaagtggg	aaactttgaa	gctgccgtgc	atttctacgg	420
aaaagccatc	gagctcaacc	cagccaacgc	cgtctatttc	tgcaacagaa	gcc	473

<210> 55

<211> 365

17

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(365)

<223> n = A,T,C or G

<400> 55

gaattcggca	cgagtgattg	aggatcagtt	gggtgccaga	cactctotta	ggtgtcagag	60
ctccagttta	cattacacag	ataaggtccc	tgccccccag	cgaagctggc	attaaagtca	120
gcaaatataat	gttcaggatt	ttgataagtg	ctgtaaaagga	aaaaagacct	gtaacagggg	180
ggaatgactg	gggagggggc	gaggctctat	ctaggcaggg	atggaccaga	cntgagagtg	240
accaggaggt	togagccagt	tgcagaggga	caagaaaggc	cttctgggca	ggggcactta	300
cagggtacaga	gcccctgcag	cagaataagc	ttctcctacc	ggagaggcaa	aaagaaggcc	360
ttttg						365

<210> 56

<211> 517

<212> DNA

<213> Homo sapien

<400> 56

gaattcggca	cgaggggacgc	cgctttgttg	cctgagatga	agttggagcc	cttgtttttg	60
acattggatc	ctatactgtg	agagctgggt	atgctgggtga	ggactgcccc	aaggtggatt	120
ttcctacagc	tattgggtatg	gtggtagaaa	gagatgacgg	aagcacatta	atggaaatag	180
atggcgataa	aggcaaacaa	ggcgggtccca	cctactacat	agataactaat	gctctgcgtg	240
ttccgagggga	gaatatggag	gccatttcac	ctctaaaaaa	tgggatgggt	gaagactggg	300
atagttttcc	agctattttg	gatcatacct	acaaaatgca	tgtcaaataca	gaagccagtc	360
tccatcctgt	tctcatgtca	gaggcaccgt	ggaataactag	agcaaagaga	gagaaactga	420
cagagttaat	gtttgaacac	tacaacatcc	ctgccttctt	cctttgcaaa	actgcagttt	480
tgacagcatt	tgctaattggt	ccgttctact	gggcttg			517

<210> 57

<211> 237

<212> DNA

<213> Homo sapien

<400> 57

gaattcggca	cgagctatga	gatagtatta	agcaattaaa	agaatatatg	acttttctac	60
atcaaaattt	gaaacttctg	tgcatcaaag	gacacaatca	acagagtga	gaggaaactt	120
acagaatggg	agaaaatatt	tgtaaatcat	gtatctcata	aggattaata	tccaggctat	180
gtaaagaact	acatctcaac	acaaaaacac	aaacagcttg	attaaaaaat	gggcaaa	237

<210> 58

<211> 485

<212> DNA

<213> Homo sapien

<400> 58

gaattcggca	cgagcgcggc	ggtcactgcg	ccggggtagt	gggccccagt	gttgcgctct	60
ctggccggtt	cttacacttt	gcttcaggct	ccagtgcagg	ggcgtagtgg	gatatggcca	120
actcgggctg	caaggacgtc	acgggtccag	atgaggagag	ttttctgtac	tttgccctacg	180
gcagcaacct	gctgacagag	aggatccacc	tccgaaaccc	ctcggcgggc	ttcttctgtg	240
tggcccgctt	gcaggatttt	aagcttgact	ttggcaattc	ccaaggcaaa	acaagtcaaa	300
cttggcatgg	agggatagcc	accatttttc	agagtcctgg	cgatgaagtg	tggggagtag	360
tatggaaaat	gaacaaaagc	aatttaaatt	ctctggatga	gcaagaaggg	gttaaaagt	420
gaaatgtatg	ttgtaataga	agttaaaagt	tgccaacttc	aagaaaggaa	aaaaaaaata	480
acctg						485

18

<210> 59
 <211> 514
 <212> DNA
 <213> Homo sapien

<400> 59
 gaattcggca cgagtggcgt tggaggtcgg cgatatggaa gatgggcagc tttccgactc 60
 ggattccgac atgacgggtcg caccacagca caggccgctg caattgccaa aagtgctagg 120
 tggcgacagt gctatgaggg ccttccagaa cacggcaact gcatgtgcac cagtatcaca 180
 ttatcgagct gttgaaagtg tggattcaag tgaagaaagt tttcttgatt cagatgatga 240
 tagctgtcct tggaaacgca aacgacagaa atgttttaac cctcctocca aaccagagcc 300
 ttttcagttt ggccagagca gtcagaaacc acctgttgct ggaggaaaga agattaacaa 360
 catatggggg gctgtgctgc aggaacagaa tcaagatgca gtggccactg aacttggtat 420
 cttgggaatg gagggcacta ttgacagaag cagacaatcc gagacctaca attatttgct 480
 tgccaagaaa cttaggaagg aatctcaaga gcat 514

<210> 60
 <211> 336
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(336)
 <223> n = A,T,C or G

<400> 60
 gaattcggca cgaggccgcc ggggtgctggt caccgggggca ggcaaaggta tagggcgcg 60
 cacgggtccag gcgctgcacg cgacgggctg gcgggtggtg gctgtgagcc ggactcaggc 120
 ggatcttgac agccttgtcc gcgagtggcc ggggatagaa cccgtgtgcg tggacctggg 180
 tgactgggag gccaccgagc gggcgctggg cagcgtgggc cccgtggacc tgctggtgaa 240
 caacgcccgt gtcgccctgc tgcagccctt nctggaggtc accaaggagg cttttgacag 300
 atcctttgag gtgaacctgc gtgcggtcat ccaggt 336

<210> 61
 <211> 515
 <212> DNA
 <213> Homo sapien

<400> 61
 gaattcggca cgaggtcgcc tgagaggtat cacctcttct gggctcaaga tggacaacaa 60
 gaagcgccctg gcctacgcca tcatccagtt cctgcatgac cagctccggc acgggggcct 120
 ctgctccgat gctcaggaga gcttggaagt cgccatccag tgcctggaga ctgcgtttgg 180
 ggtgacggta gaagacagtg accttgcgct ccctcagact ctgccggaga tatttgaagc 240
 ggctgccacg ggcaaggaga tgccgcagga cctgaggagc ccagcgcgaa cccgccttc 300
 cgaggaggac tcagcagagg cagagcgcc caaaaccgaa ggaaacgagc agatgaaagt 360
 ggaaaacttt gaagctgccc tgcatttcta cggaagagcc atcgagctca acccagccaa 420
 cgccgtctat ttctgcaaca gagccgcagc ctacagcaaa ctccggcaact acgcaggcgc 480
 ggtgcaggac tgtgagcggg ccatctgcat tgacc 515

<210> 62
 <211> 417
 <212> DNA
 <213> Homo sapien

<400> 62
 gaattcggca cgagagccaa cctcctggaa gggcacgctg gtgctgaggt gtacccttca 60
 gccaaagccaa tgatcaaatt ccaatcacc tatgaggaa agttggaaca gcagagactg 120

19

gcagtgcagc	aggtggagga	ggcccagcag	ctgcgggaac	accaggaagc	tttgcaccag	180
cagaggctgc	aggggcactt	actacggcag	caggaacagc	agcagcagca	ggtggcaaga	240
gagatggccc	tgagaggca	ggctgagctt	gaggagggcc	ggccgcagca	ccaggagcag	300
ctccggcagc	aagctcatta	tgatgctatg	gataatgata	tcgttcaggg	agcagaggac	360
cagggaatcc	aaggagagga	aggagcctat	gaaagagaca	accagcacca	agatgaa	417

<210> 63
 <211> 455
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(455)
 <223> n = A,T,C or G

<400> 63						
gaattcggca	cgagggccgg	gcttgggctg	cgtggagaat	actttttgcg	atgcctactg	60
gagactttga	ttcgaagccc	agttgggccc	accaggtgga	ggaggagggg	gaggacgaca	120
aatgtgtcac	cagcgagctc	ctcaagggga	tccctctggc	cacaggtgac	accagcccag	180
agccaganct	actgccggga	gctccactgc	cgcctcccaa	ggaggtcatc	aacggaaaca	240
taaagacagt	gacagagtac	aagatagatg	aggatggcaa	gaagttcaag	attgtccgca	300
ccttcaggat	tgagaccggg	aaggcttcaa	aggctgtcgc	aaggaggaag	aactggaaga	360
agttcgggaa	ctcagagttt	gacccccccg	gacccaatgt	ggccaccacc	actgtcagtg	420
acgatgtctc	tatgacgttc	atcaccagca	aagag			455

<210> 64
 <211> 517
 <212> DNA
 <213> Homo sapien

<400> 64						
gaattcggca	cgagccatgt	tggggtttgt	gggtcgggtg	gccgctgctc	cgccctccgg	60
ggccttgccg	agactcacc	cttcagcgtc	gctgccccca	gctcagctct	tactgcgggc	120
cgctccgacg	gcggtccatc	ctgtcaggga	ctatgcggcg	caaacatctc	cttcgccaaa	180
agcaggcgcc	gccaccgggc	gcatcgtggc	ggtcattggc	gcagtgggtg	acgtccagtt	240
tgatgaggga	ctaccaccaa	ttctaaatgc	cctggaagtg	caaggcaggg	agaccagact	300
ggttttggag	gtggcccagc	atltgggtga	gagcacagta	aggactattg	ctatggatgg	360
tacagaaggc	ttggttagag	gccagaaagt	actggattct	ggtgcaccaa	tcaaaattcc	420
tgttggctct	gagactttgg	gcagaatcat	gaatgtcatt	ggagaaccta	ttgatgaaag	480
aggtcccatc	aaaaccaaac	aatttgctcc	cattcat			517

<210> 65
 <211> 519
 <212> DNA
 <213> Homo sapien

<400> 65						
gaattcggca	cgagtggagg	tcggcgatat	ggaagatggg	cagctttccg	actcggattc	60
cgacatgacg	gtcgcaccca	gcgacaggcc	gctgcaattg	ccaaaagtgc	taggtggcga	120
cagtgcctatg	agggccttcc	agaacacggc	aactgcatgt	gcaccagtat	cacattatcg	180
agctgttgaa	agtgtggatt	caagtgaaga	aagtttttct	gattcagatg	atgatagctg	240
tctttggaaa	cgcaaacgac	agaaatgttt	taacctctct	cccaaaccag	agccttttca	300
gtttggccag	agcagtcaga	aaccacctgt	tgctggaggga	aagaagatta	acaacatatg	360
gggtgctgtg	ctgcaggaac	agaatcaaga	tgcatgtggc	actgaacttg	gtatcttggg	420
aatggagggc	actattgaca	gaagcagaca	atccgagacc	tacaattatt	tgcttgccaa	480
gaaacttagg	aaggaatctc	aagagcattc	caaaagatc			519

<210> 66

20

<211> 517
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(517)
 <223> n = A,T,C or G

<400> 66
 gaattcggca cgagggcggc tgaggaaagc aggaggaggt ggcggcggcg ggaagatggc 60
 tccttcacct accaaacgca aagaccgctc agatgagaag tccaaggatc gctcaaaaga 120
 taaaggggccc accaaggagt cgagtgaaga ggatcgcggc cgggacaaaa ccgaaaagag 180
 gcgcagcgct tccagtggta gcagcagtac caggtctcgg tcagctcga cttccagctc 240
 aggtctccagc accagcactg gctcaagcag tggctccagc tcttctcag catccagccg 300
 ctcaggaagc tccagcacct cccgcagctc cagctctagc agctcttctg gctctccaag 360
 tcctttctcgg cgcanacacg acaacaggag gcgctccgc tccaaatcca aaccacctaa 420
 aagagatgaa aaggagagga aaaggcggag cccatctcct aagcccacca aagtgcacat 480
 tgggagactc acccggaatg tgacaaagga tcacatc 517

<210> 67
 <211> 517
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(517)
 <223> n = A,T,C or G

<400> 67
 gaattcggca cgagggcgccg tgcagcggtc gagtgtnnngc ggcggcgacg gcaaaccgcg 60
 agctgcgggc cggcgcgccg gaggaggacg cgggtgcggc ctaggaaacg gagctgcggg 120
 cggaggctcc atgttgaggaa gcggcgccgt tcgtgcttgt tagcggaat ccgggagccg 180
 cgggggtgagc tggcgggggc cgggccctaa gtgaagatgg agggcccgct gcggcctgcc 240
 gcggacatcc tgaggcgga cccgcagcag gactacgaac tcgtccagag ggtcggcagc 300
 ggcacctacg gggacgtcta taaggccaga aatgtacaca caggagagct ggctgcagta 360
 aaaatcatta aattggagcc tggagatgat ttttctttga ttcaacaaga aatatttatg 420
 gttaaagaat gtaaacattg taacatcggt gcctactttg ggagttatct tagtcgggaa 480
 aaactatgga tttgtatgga atactgtggt ggcggtat 517

<210> 68
 <211> 516
 <212> DNA
 <213> Homo sapien

<400> 68
 gaattcggca cgaggtcggc tcctgctatt ccggtttctc cactccgtcc cccgcgggtc 60
 tgctctgtgt gccatggacg gcattgtccc agatatagcc gttggtacaa agcggggatc 120
 tgacgagctt ttctctactt gtgtcactaa cggaccgttt atcatgagca gcaactcggc 180
 ttctgcagca aacggaaatg acagcaagaa gttcaaaggt gacagccgaa gtgcaggcgt 240
 cccctctaga gtgatccaca tccgggaagc ccccatcgac gtcacggagg gggaaagtc 300
 ctccctgggg ctgccctttg ggaagggtcac caacctcctg atgctgaagg ggaaaaacca 360
 ggccttcacg gagatgaaca cggaggaggc tgccaacacc atggtgaact actacacctc 420
 ggtgaccctt gtgctgcgcg gccagcccat ctacatccag ttctccaacc acaaggagct 480
 gaagaccgac agctctccca accaggcgcg ggccca 516

<210> 69
 <211> 455

21

<212> DNA

<213> Homo sapien

<400> 69

gaattcggca	cgaggagcca	tagagcctct	gcctc gatgc	cgtttttgcc	ccgctctttg	60
gacacgccga	cccggcgctc	cccaaggaa	gctgtcccaa	caagattccc	gtgaaagagc	120
accggtgtcg	ccccctcccg	tggactttctg	tgccgccccg	tccacacctg	ttcttggtg	180
catgtgggtt	ttcggttcct	ggcgggtccag	gacggggcgg	gggctccct	cccatctcgt	240
gctgggaggt	ctcagcgcg	tctcctgtcc	ctgggacgtg	cgtctctcct	tctcatgccg	300
ttctggaaaa	tgctcttgct	gtagagagca	gctgcttctg	ccaggtgtt	ggaggtggtg	360
gagcgcttc	cgattccatt	catggcattt	tgtgatgtga	tgtaattgga	atagagctgt	420
tgatttaagg	caaaaaaaaa	aaaaaaaaaac	tcgag			455

<210> 70

<211> 569

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(569)

<223> n = A,T,C or G

<400> 70

gaattcggca	cgagcagaac	gcagctctgc	tctgctngag	gaggtgcaga	gcctccggga	60
ggaggctgag	aaacagcggg	tggcttcaga	gaacctgcgg	caggagctga	cctcacaggc	120
tgagcgtgag	gaggagctgg	gccaagaatt	gaaggcgtgg	caggagaagt	tcttcagaa	180
agagcaggcc	ctctccaccc	tgagctcga	gcacaccagc	acacaggccc	tggtgagtga	240
gctgctgcca	gctaagcacc	tctgccagca	gctgcaggcc	gagcaggccg	ctgccagaa	300
acgccaccgt	gaggagctgg	agcagagcaa	gcaggccgct	gggggactgc	gggcagagct	360
gctgcgggcc	cagcgggagc	ttggggagct	gattcctctg	oggcagaagg	tgccagagca	420
ggagcgaaca	gctcagcagc	tgcgggcaga	gaaggccagc	tatgcagagc	agctgagcat	480
gctgaagaag	gcgcattggc	tgctggcaga	ggagaaccgg	gggctgggtg	agcgggcaa	540
ccttggccgg	cagtttctgg	aagtggagt				569

<210> 71

<211> 555

<212> DNA

<213> Homo sapien

<400> 71

gaattcggca	cgagtggcga	cgccccctaa	gcggcgggcg	gtggaggcca	cgggggagaa	60
agtgtgtcgc	tacgagacct	tcatcagtga	cgtgtgtcag	cgggacttgc	gaaagtgct	120
ggaccatcga	gacaaggtat	atgagcagct	ggccaaatac	cttcaactga	gaaatgtcat	180
tgagcgactc	caggaagcta	agcaactcga	gttatatatg	caggtggatt	tggtgtgtaa	240
cttcttcggt	gacacagtgg	tcccagatac	ttcacgcata	tatgtggccc	tggtatattg	300
ttttttcctg	gagttgacac	tgccagaagc	tctcaagttc	attgatcgta	agagctctct	360
cctcacagag	ctcagcaaca	gcctcaccaa	ggactccatg	aatatcaaag	cccatatcca	420
catgttgcta	gaggggctta	gagaactaca	aggcctgcag	aatttcccag	agaagcctca	480
ccattgactt	cttcccccca	tcctcagaca	ttaaagagcc	tgaatgccaa	aaaaaaaaaa	540
aaaaaaaaaac	tcgag					555

<210> 72

<211> 567

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

22

<222> (1)...(567)

<223> n = A,T,C or G

<400> 72

gaattcggca	cgagggctgg	tggagttgtt	agtgtncat	ggcaacacct	tctttgtggt	60
tctcattgtc	atccttgtgc	tgttggcat	cgatgccgtg	cgcgaaattc	ggaagtatga	120
tgatgtgacg	gaaaagggtga	acctccagaa	caatcccggg	gccatggagc	acttccacat	180
gaagcttttc	cgtgcccgaga	ggaatctcta	cattgctggc	ttttccttgc	tgctgtcctt	240
cctgcttaga	cgcctgggtga	ctctcatttc	gcagcaggcc	acgctgctgg	cctccaatga	300
agcctttaaa	aagcaggcgg	agagtgcctg	tgaggcgcc	aagaagtaca	tgaggagaa	360
tgaccagctc	aagaagggtg	ctgctgttga	cggaggcaag	ttggatgtcg	ggaatgctga	420
ggtgaagttg	gaggaagaga	acaggagcct	gaaggctgac	ctgcagaagc	taaaggacga	480
gctggccagc	actaagcaaa	aactagagaa	agctgaaaac	caggttctgg	ccatgcggaa	540
gcagtctgag	ggcctcacca	aggagta				567

<210> 73

<211> 254

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(254)

<223> n = A,T,C or G

<400> 73

gaattcggca	cgagcctgga	caaggagaga	gtgcgntgc	tgagagccga	gccagcaat	60
cccgatcctc	tgagtcgtga	agaaggagg	cagcgagggg	gttgggggtg	ggcctgagg	120
caagccccc	ggctccgctc	ttgccagagg	gacaggagcc	atggctcaga	aaatggactg	180
tggtgcgggc	ctcctcggtc	tccaggctga	ggcctccgta	gaagacagcg	ccttgcttat	240
gcagaccttg	atgg					254

<210> 74

<211> 516

<212> DNA

<213> Homo sapien

<400> 74

gaattcggca	cgagcagccc	tgggctgagc	cgcgccgcac	catgcccgcc	gtggacaagc	60
tcctgctaga	ggaggcggtg	caggacagcc	cccagactcg	ctctttactg	agcgtgtttg	120
agaagatgc	tggcaccctc	acagactata	ccaaccagct	gctccaggca	atgcagcgcg	180
tctatggagc	ccagaatgag	atgtgcctgg	ccacacaaca	gctttctaag	caactgctgg	240
catatgaaaa	acagaacttt	gctcttggca	aagggtgatga	agaagtaatt	tcaacactoc	300
actatttttc	caaagtgggtg	gatgagctta	atcttctcca	tacagagctg	gctaaacagt	360
tggcagacac	aatgggttcta	cctatcatac	aattccgaga	aaaggatctc	acagaagtaa	420
gcacttttaa	ggatctattt	ggactcgcta	gcaatgagca	tgacctctca	atggcaaaat	480
acagcaggct	gcctaagaaa	aaggagaatg	agaagg			516

<210> 75

<211> 468

<212> DNA

<213> Homo sapien

<400> 75

gaattcggca	cgagcaggga	cgacgccag	aatgggagct	gactgatatg	gtgggtgtggg	60
tgactggagc	ctcgagtgga	attgggtgag	agctggctta	ccagtgtctt	aaactaggag	120
tttctcttgt	gctgtcagcc	agaagagtgc	atgagctgga	aagggtgaaa	agaagatgcc	180
tagagaatgg	caattttaaa	gaaaaagata	tacttgTTTT	gcccttgac	ctgaccgaca	240
ctgggttccca	tgaagcggct	accaaagctg	ttctccagga	gtttggtaga	atcgacattc	300

23

tggtcaacaa	tggtggaatg	tcccagcggt	ctctgtgcat	ggataccagc	ttggatgtct	360
acagaaagct	aatagagctt	aactacttag	ggacgggtgc	cttgacaaaa	tgtgttctgc	420
ctcacatgat	cgagaggaag	caaggaaaga	ttgttacttg	tgaatagc		468

<210> 76
 <211> 349
 <212> DNA
 <213> Homo sapien

<400> 76						
gaattcggca	cgagctcgac	tcttagcttg	tcggggacgg	taaccgggac	cgggtgtctg	60
ctcctgtcgc	cttcgcctcc	taatccctag	ccactatgcg	tgagtgcac	tccatccacg	120
ttggccaggc	tggtgtccag	attggcaatg	cctgtcggga	gctctactgc	ctggaacacg	180
gcattccagcc	cgatggccag	atgccaaagt	acaagaccat	tgggggagga	gatgactcct	240
tcaacacctt	cttcagttag	acgggcgctg	gcaagcacgt	gccccgggct	gtgtttgtag	300
acttgggaacc	cacagtcatt	gatgaagttc	gcactggcac	ctaccgcca		349

<210> 77
 <211> 469
 <212> DNA
 <213> Homo sapien

<400> 77						
ataggcacat	acacatacac	agtctcagca	aggttataaa	gaaccctgtc	aggtocactt	60
gcaacatggc	cttgctactt	ggattagctc	ctttaagcct	gaaaataact	ttcctgggtca	120
tggaagaact	ggacgcactc	tttaacttat	gaaatagaag	ttgaacttga	aaactctttt	180
taaaaaatcc	tggttttgca	ggacagctac	ataatgaatg	tatatattaa	gactgtagct	240
gaattgcaca	tgaaatcaga	ttgccaaact	cttgactttc	aatgttagac	atttatcctt	300
aagttgtgag	cgatatatgt	agcatgctgt	gaaatgtctg	ttatagctct	ttaattcatc	360
agtattaata	cagaattatc	atttgcgttt	cttggtactt	tttattcaat	gtaatcagaa	420
gctgtgatgt	tttgcccttg	tagtcctgtg	ctttggtact	gtaattttt		469

<210> 78
 <211> 399
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(399)
 <223> n = A,T,C or G

<400> 78						
gcgctcgggt	tgagggctcg	gcgcgggggt	tcctgttctt	tcttctgcgc	ggctgcagct	60
cggaacttcg	gcctgaccga	gccccatgg	cttcagaaga	gctacagaaa	gatctagaag	120
aggtaaagg	gttgctggaa	aaggctacta	ggaaaagagt	acgtgatgcc	cttacagctg	180
aaaaatccaa	gattgagaca	gaaatcaaga	acaagatgca	acagaaatca	cagaagaaag	240
canaacttct	tgataatgaa	aaaccagctg	ctgtgggttg	tcccattaca	acgggctata	300
cggtgaaaat	cagtaattat	ggatgggata	aagtcagata	agtttgtgaa	aatctacatt	360
accttaactg	gagttcatca	agttccact	gagaatgtg			399

<210> 79
 <211> 439
 <212> DNA
 <213> Homo sapien

<400> 79						
ccgagaagct	gggctttgct	ggtcttgtac	aggagatctc	atttgggaca	actaaggata	60
aatgctggt	catcgagcag	tgtaagaact	ccagagctgt	aaccattttt	attagaggag	120

24

gaaataagat	gatcattgag	gaggcgaaac	gatcccttca	cgatgctttg	tgtgtcatcc	180
ggaacctcat	ccgcgataat	cgtgtgggtg	atggaggagg	ggctgctgag	atatacctgtg	240
ccctggcagt	tagccaagag	gcggataagt	gccccacctt	agaacagtat	gccatgagag	300
cgtttgccga	cgcactggag	gtcatcccca	tggccctctc	tgaaaacagt	ggcatgaatc	360
ccatccagac	tatgaccgaa	gtccgagcca	gacaggtgaa	ggagatgaac	cctgctcttg	420
gcatcgactg	tttgcacaa					439

<210> 80

<211> 437

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(437)

<223> n = A,T,C or G

<400> 80

aattaacatc	ttttttgttt	aggcatgttc	aattaatgct	gtagctatca	tagctntgct	60
cttacctgaa	gccttgtccc	caccacacag	gacagccttc	ctcctgaaga	gaatgtcttt	120
gtgtgtccga	agttgagatg	gcctgcccta	ctgccaaaga	ggtgacagga	aggctgggag	180
cagctttgtt	aaattgtgtt	cagttctgtt	acacagtgc	ttgccctttg	ttgggggtat	240
gcatgtatga	acacacatgc	ttgtcggaac	gctttctcgg	cgtttgtccc	ttggctctca	300
tctcccccat	tcctgtgcct	actttgcctg	agttcttcta	cccccgagc	tgccagccac	360
attgggagtc	tgtttgttcc	agtgggggtg	agctgtcttt	gtcgtggaga	tcttggaaact	420
ttgcacatgt	cactact					437

<210> 81

<211> 472

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(472)

<223> n = A,T,C or G

<400> 81

atattttant	aatgcagagc	tatagtctca	attgttactt	tataagggtg	ttttattaac	60
aaacccaaat	cctggatttt	cctgtctttg	ctgtattttg	aaaaacacgt	gttgactcca	120
ttgttttaca	tgtagcaaag	tctgccatct	gtgtctgctg	tattataaac	agataagcag	180
cctacaagat	aactgtattt	ataaaccact	cttcaacagc	tggctccagt	gctgggttta	240
gaacaagaat	gaagtcatct	tggagtcctt	catgtctaaa	agattttaagt	taaaaacaaa	300
gtgttacttg	gaaggtttag	ttctatcatt	ctggatagat	tacagatata	ataaccatgt	360
tgactatggg	ggagagacgc	tgcattccag	aaacgtctta	acacttgagt	gaatcttcaa	420
aggaccctga	cattaaatgc	tgaggcttta	atacacacat	attttatccc	aa	472

<210> 82

<211> 448

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(448)

<223> n = A,T,C or G

<400> 82

gttcagtgn	gccctcagag	ctottgctgt	tagctggcag	ctgacgctgc	taggatagtt	60
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25

agtttggaaa	tggtacttca	taataaacta	cacaaggaaa	gtcagccacc	gtgtcttatg	120
aggaattgga	cctaataaat	tttagtgtgc	cttccaaacc	tgagaatata	tgcttttgga	180
agttaaaatt	taaatggcct	ttgccacata	catagatcct	catgatgtgt	gagtgttaatt	240
ccatgtggat	atcagttacc	aaacattaca	aaaaaatttt	atggcccaaa	atgaccaacg	300
aaattgttac	aatagaattt	atccaatttt	gatcttttta	tattcttcta	ccacacctgg	360
aaacagacca	atagacattt	tggggtttta	taatgggcat	ttgtataaag	cattactctt	420
tttcaataaa	ttgtttttta	atttaaaa				448

<210> 83
 <211> 270
 <212> DNA
 <213> Homo sapien

<400> 83	
cagtgtggtg	gaattaatca
agtggtttat	gggggctagc
ggtgttttag	aaaatgtggg
aagcactcac	ctacacgttt
ataaaatggt	atttttaaa

<210> 84
 <211> 359
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(359)
 <223> n = A,T,C or G

<400> 84	
tccaaagtta	gacaaaatgc
aaccactcat	tcacttctag
ggatatgaaa	gcatacctga
caagtccaag	gatgtacttt
acttcttgcc	aaccaaaactg
tgaggagaat	attgagttct

<210> 85
 <211> 371
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(371)
 <223> n = A,T,C or G

<400> 85	
ctgcagcccg	ggggatccac
ctgtatccag	cgccaggtcc
ttcggcccg	gctaagttag
atacctgctg	ttcggattta
tggaactatg	ctccgattcg
taataattcc	agcttctaca
tgcttggtgg	g

<210> 86
 <211> 500

26

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(500)
<223> n = A,T,C or G

<400> 86
ctgcagcccg ggggatccac tagtttncta tgatcattaa actcattctc agggttaaga 60
aaggaatgta aatttctgcc tcaatttgta cttcatcaat aagtttttga agagtgcaga 120
tttttagtca ggtcttaaaa ataaactcac aaatctggat gcattttctaa attctgcaaa 180
tgtttcctgg ggtgacttaa caaggaataa tcccacaata tacctagcta cctaatacat 240
ggagctgggg ctcaaccacac tgtttttaag gatttgcgct aacttggggc tgaggaaaaa 300
taagtagtnc gaggaagtag tttttaaatg tgagcttata gatanaaaca gaatatcaac 360
ttaattatga aattgttaga acctgttctc ttgtatctga atctgattgc aattactatt 420
gtactgatag actccagcca ttgcaagtct cagatatctt agctgtgtag tgattcttga 480
aattcttttt aagaaaaatt 500

<210> 87
<211> 550
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(550)
<223> n = A,T,C or G

<400> 87
ctgcagcccg ggggatccac tagtccantg tgggtgaatt ccaggaactg gaccaggunc 60
tggagcggat ctccaccatg cgccttccgg atgagcgggg cctctctggag cacctctact 120
ccctgcacat ccccaactgt gacaagcatg gcctgtacaa cctcaaacag tgcaagatgt 180
ctctgaacgg gcagcgtggg gagtgtcgtg gtgtgaaccc caacaccggg aagctgatcc 240
agggagcccc caccatccgg ggggaccccg agtgtcatct cttctacaat gaggcagcagg 300
aggctcgcgg ggtgcacacc cagcggatgc agtagaccgc agccagccgg tgcctggcgc 360
ccctgcccc cgccctctc caaacaccgg cagaaaacgg agagtgcctg ggtggtgggt 420
gctggaggat tttccagttc tgacacacgt atttatatat ggaaagagac cagcaccgag 480
ctcggcacct ccccggcctc tctcttccca ngctgcagat gccacacctg ctccctcttg 540
ctttcccccg 550

<210> 88
<211> 429
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(429)
<223> n = A,T,C or G

<400> 88
gggaccagac tcgtctcagg ccanttgacg ccttctcagc caaacgccga ccaaggaaaa 60
ctcactacca tgagaattgc agtgatttgc ttttgcctcc taggcatcac ctgtgccata 120
ccagttaaac aggctgattc tgggaagttct gaggaaaagc agctttacaa caaataccca 180
gatgctgtgg ccacatggct aaaccctgac ccatctcaga agcagaatct cctagcccca 240
cagaatgctg tgtcctctga agaaaccaat gacttttaac aagagaccct tccaagtaag 300
tccaacnaaa gccatgacca catggatgat atggatgatg aagatgatga tgaccatgtg 360
gacagccagg actccattga ctggaacnac tctgatgatg tanatgacac tgatgattct 420

caccagtct

429

<210> 89

<211> 477

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(477)

<223> n = A,T,C or G

<400> 89

ttttaatttta	caccaagaac	ttctcaataa	aagaaaatca	tgaatgctcc	acaatttcaa	60
cataccacaa	gagaagttaa	tttcttaaca	ttgtgttcta	tgattatttg	taagaccttc	120
accaagtict	gatatctttt	aaagacatag	ttcaaaattg	cttttgaaaa	tctgtattct	180
tgaaaatata	cttgttgtgt	attaggtttt	taaataccag	ctaaaggatt	acctcactga	240
gtcatcaggt	accctcctat	tcagctcccc	aagatgatgt	gtttttgctt	accctaagag	300
aggntttctt	cttattttta	gataattcaa	gngcttagat	aaattatgtt	ttctttaagt	360
gtttatggta	aactctttta	aagaaaattt	aatatgttat	agctgaatct	ttttggtaac	420
tttaaattctt	tatcatagac	tctgtacata	tgttcaaatt	agctgcttgc	ctgatgt	477

<210> 90

<211> 310

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(310)

<223> n = A,T,C or G

<400> 90

ctgcagcccg	ggggatccac	tagtcanttt	attgacacta	tttgaaactt	ttgaaatata	60
aacggagagg	ctttctgttg	agacattgtc	acaaaaacaa	ttttttgaaa	tgttcctgaa	120
actaatttgg	gtttaaagat	taaaagggtt	gttaccattc	ttatctgagt	agttgggagg	180
aggggaatac	cactttagtt	catttggaaa	atatagacat	atttcttttg	ctttcttaaa	240
acagcttaaa	atgatgaact	tttataattt	taatttgaag	attgaataaa	tattttttat	300
aaagataaaa						310

<210> 91

<211> 532

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(532)

<223> n = A,T,C or G

<400> 91

ctgcagcccg	ggggatccac	tagtcatgat	gtgtgttgta	ttttaaaaaat	tatctgcaac	60
cttaattcag	ctgaagtact	ttatatattca	aaagaatgaa	taacattgat	aataaaatcg	120
ctactttaag	gggtttgtcc	aaaataaata	ttgtggcctt	atatatcaca	ctattgtaga	180
aagtattatt	taattttaa	ggatgcaggt	tgtctactaa	agaaagatta	tatataacta	240
tgctaattgt	tcataatcaa	cagaaaccaa	gatagagcta	caaactcagc	tgtacagttc	300
gtacactaaa	ctcttcttgc	ttttgcatta	taaggaatta	agtctccgat	tattaggtga	360
tcacctgga	tgatcagttt	tctgctgaag	gcacctactc	agtatctttt	cctctttatc	420
actctgcatt	ggtgaattta	atcctctcct	ttgtgttcaa	cttttgtgtg	cttttaaaat	480

28

cagcttttatt ctaaagcaaa tctgtgtcta ctttaaaaaa ctgnaaatgg aa 532

<210> 92
 <211> 608
 <212> DNA
 <213> Homo sapien

<400> 92
 cactactgtc ttctccttgt agctaataca tcaatattct tcccttgct gtgggcagtg 60
 gagagtgtcg ctgggtgtac gctgcacctg cccactgagt tggggaaaga ggataatcag 120
 tgagcactgt tctgctcaga gctcctgac taccacccc cctaggatcc aggactgggt 180
 caaagctgca tgaaaccagg ccctggcagc aacctgggaa tggctggagg tgggagagaa 240
 cctgacttct ctttccctct ccctcctcca acattactgg aactctatcc tgttaggac 300
 ttctgagctt gtttccctgc tgggtgggac agaggacaaa ggagaaggga gggctagaa 360
 gaggcagccc ttctttgtcc tctggggtaa atgagcttga cctagagtaa atggagagac 420
 caaagcctc tgatttttaa tttccataaa atgttagaag tatatatata catatatata 480
 tttcttttaa tttttgagtc tttgatattgt ctaaaaatcc attccctctg ccctgaagcc 540
 tgagtggagac acatgaagaa aactgtgttt catttaaaaga tgtaattaa atgattgaaa 600
 cttgaaaa 608

<210> 93
 <211> 519
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (519)
 <223> n = A,T,C or G

<400> 93
 ctgcagcccc ggggatccac tagtccagtg tgggtggaatt ctaaagaagt aggtgctgca 60
 cacaatatg taaagcaatt gtaggaaatt tgaaaggaaa aaaagaaacc gaagccagta 120
 ttttaataat tgctttttct gtgtattttg tattgggctg ggggatagca tcaaagggtg 180
 aactttttga gctttctatg aaaaacccca ggaccttctt tctttggcca tttctatgga 240
 aatgcgatgt cagatggatg gtaatggtgc cctccagtgg ctgtgagacc tcattgcgca 300
 ttgtctactg gagcttttagt cttctgagac ggaggaaaac tgctgaatac tctggattca 360
 tctatgtcta caatgttgca tttatgaaaa actacactgn gctaggcgca ttctaggaca 420
 tgaatatgac cacaccctct ttcaccgggt gtttctgtag caagttttca tattcttttc 480
 aaacaatggt ttctctgcgt taattattga ggaaaaaaa 519

<210> 94
 <211> 569
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (569)
 <223> n = A,T,C or G

<400> 94
 ctgcagcccc ggggatccac tagtccantg tgggtggaatt cgtctgcgag ccaggattcc 60
 cgatccagag acaatggccc cgatgggatg gagccgaag gcgtcatcga gagtaactgg 120
 aatgagattg ttgacagctt tgatgacatg aacctctcgg agtcccttct ccgtggcatc 180
 tacgcctatg gttttgagaa gccctctgcc atccagcagc gagccattct acctgtatc 240
 aagggttatg atgtgattgc tcaagcccaa tctgggactg ggaaaacggc cacatttgcc 300
 atatcgattc tgcagcagat tgaattagat ctnaaagcca cccaggcctt ggtcctagca 360
 cccactcgag aattggctca gcagatacag aagggtggtcn tggcactagg agactacatg 420

29

ggcgccctcct	gtcacgcctg	tatcgggggc	accaacgtgc	gtgctgaggt	gcagaaactg	480
cagatggaag	ctccccacat	catcggtggg	acccctggcc	gtgtgtttga	tatgcttaac	540
cggagatacc	tgtcccccaa	atacatcaa				569

<210> 95
 <211> 260
 <212> DNA
 <213> Homo sapien

<400> 95						
gacaagctcc	tgggtcttgag	atgtctttctc	gttaaggaga	tgggcctttt	ggaggtaaag	60
gataaaatga	atgagttctg	tcatgattca	ctattctaga	acttgcatga	cctttactgt	120
gttagctctt	tgaatgttct	tgaaatttta	gactttcttt	gtaaacaaat	gatatgtcct	180
tatcattgta	taaaagctgt	tatgtgcaac	agtgtggaga	ttccttgtct	gatttaataa	240
aataacttaaa	cactgaaaaa					260

<210> 96
 <211> 438
 <212> DNA
 <213> Homo sapien

<400> 96						
atttctcttt	agttctttgc	aagaaggtag	agataaagac	actttttcaa	aaatggcaat	60
ggtatcagaa	ttcctcaagc	aggcctggtt	tattgaaaat	gaagagcagg	aatatgttca	120
aactgtgaag	tcatccaaaag	gtgggtcccg	atcagcgggtg	agccctatc	ctaccttcaa	180
tccatcctcg	gatgtcgctg	ccttgcataa	ggccataatg	gttaaagggtg	tggatgaagc	240
aaccatcatt	gacattctaa	ctaagcgaaa	caatgcacag	cgtcaacaga	tcaaagcagc	300
atatctccag	gaaacaggaa	agccctgga	tgaaacactg	aagaaagccc	ttacaggtca	360
ccttgaggag	gttggttttag	ctctgctaaa	aactccggcg	caatttgatg	ctgatgaact	420
tcgttgctgc	catgaagg					438

<210> 97
 <211> 471
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(471)
 <223> n = A, T, C or G

<400> 97						
tcgttatccg	cgatnggttt	cctggcagct	acattcctgc	tcctggcgct	cagcaccgct	60
gccaggccg	aaccgggtgca	gttcaaggac	tgcgatattc	agtctaaaag	cagcaaggcc	120
gtggtgcatg	gcacccctgat	ggcgctccca	gttccctttc	ccattcctga	gcctgatggt	180
tgtaagagt	gaattaaactg	ccctatccaa	aaagacaaga	cctatagcta	cctgaataaa	240
ctaccagtga	aaagcgaata	tccctctata	aaactgggtg	tggagtggca	acttcaggat	300
gacaaaaacc	aaagtctctt	ctgctgggaa	atcccagtac	agatcgtttc	tcattctctaa	360
gtgcctcatt	gagttcggtg	catctggcca	atgagtctgc	tgagactctt	gacagcacct	420
ccagctctgc	tgcttcaaca	acagtgaact	gctctccaat	ggtatccagt	g	471

<210> 98
 <211> 578
 <212> DNA
 <213> Homo sapien

<400> 98						
ccagtgtggt	ggaattcgca	gccaccgcca	cccattggaa	tggccaacag	gggacctgca	60
tatggcctga	gccgggaggt	gcagcagaag	attgagaaac	aatatgatgc	agatctggag	120

30

cagatcctga	tccagtggat	caccacccag	tgccgaaagg	atgtgggccc	gccccagcct	180
ggacgcgaga	acttccagaa	ctggctcaag	gatggcacgg	tgctatgtga	gctcattaat	240
gcactgtacc	ccgaggggca	ggccccagta	aagaagatcc	aggcctccac	catggccttc	300
aagcagatgg	agcagatctc	tcagttcctg	caagcagctg	agcgctatgg	cattaacacc	360
actgacatct	tccaaactgt	ggacctctgg	gaaggaaaga	acatggcctg	tgtgcagcgg	420
acgctgatga	atctgggtgg	gctggcagta	gcccagatg	atgggctctt	ctctggggat	480
cccaactggt	tccctaagaa	atccaaggag	aatcctcgga	acttctcgga	taaccagctg	540
caagagggca	agaacgtgat	cgggttacag	atgggcac			578

<210> 99
 <211> 416
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(416)
 <223> n = A,T,C or G

caagaatgtg	cctaactggc	atanagatct	ggtacgagtg	tgtgaaaaca	tccccattgt	60
gntgngtggc	aacaaagtgg	atattaagga	caggaaagtg	aaggcgaaat	ccattgtctt	120
ccaccgaaag	aagaatcttc	agtactacga	catttctgcc	aaaagtaact	acaactttga	180
aaagcccttc	ctctggcttg	ctaggaagct	cattggagac	cctaacttgg	aatttgttgc	240
catgctgct	ctcgccccac	cagaagttgt	catggaccca	gctttggcag	cacagtatga	300
gcacgactta	gaggttgctc	anacaactgc	tctcccggat	gaggatgatg	acctgtgaga	360
atgaagctgg	agccancn	cagaagtcta	gttttatang	cagctgtcct	gtgatg	416

<210> 100
 <211> 441
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(441)
 <223> n = A,T,C or G

agacaatgac	cccacggntc	ctccttatga	ctccattcaa	atctacggtt	atgaaggcag	60
gggctcagtg	gccgggtccc	tgagctccct	agagtcggcc	accacagatt	cagacttgga	120
ctatgattat	ctacagaact	ggggacctcg	ttttaagaaa	ctagcagatt	tgtatggttc	180
caaagacact	tttgatgacg	attcttaaca	ataacgatac	aaatttggcc	ttaagaactg	240
tgtctggcgt	tctcaagaat	ctanaagatg	tgtaaacagg	tattttttta	aatcaaggaa	300
aggctcattt	aaaacaggca	aagttttaca	gagaggatac	atttaataaa	actgcgagga	360
catcaaagtg	gtaaataactg	tgaaatacct	tttctcacia	aaaggcaaat	attgaagttg	420
tttatcaact	tcgctagaaa	a				441

<210> 101
 <211> 521
 <212> DNA
 <213> Homo sapien

ccagcgccca	gagagacacc	agagaaccca	ccatggcccc	ctttgagccc	ctggcttctg	60
gcatcctgtt	gttgctgtgg	ctgatagccc	ccagcagggc	ctgcacctgt	gtcccacccc	120
accacagag	ggccttctgc	aattccgacc	tcgtcatcag	ggccaagttc	gtggggacac	180
cagaagtcaa	ccagaccacc	ttataccagc	gttatgagat	caagatgacc	aagatgtata	240
aagggttcca	agccttaggg	gatgcgcgtg	acatccgggt	cgtctacacc	cccgccatgg	300

31

agagtgtctg	cggatacttc	cacaggtccc	acaaccgcag	cgaggagttt	ctcattgctg	360
gaaaactgca	ggatggactc	ttgcacatca	ctacctgcag	tttcgtgggt	ccctggaaca	420
gcctgagctt	agctcagcgc	cggggcttca	ccaagacctc	caactgttggc	tgtgaggaat	480
gcacagtgtt	tccctgttta	tccatcccct	gcaaactgca	g		521

<210> 102
 <211> 520
 <212> DNA
 <213> Homo sapien

<400> 102						
gaagaaaaag	aaatttctgat	acgggacaaa	aatgctcttc	aaaacatcat	tctttatcac	60
ctgacaccag	gagttttcat	tggaaaagga	tttgaacctg	gtgttactaa	catttttaag	120
accacacaag	gaagcaaaaat	ctttctgaaa	gaagtaaata	atacacttct	ggatgaatgaa	180
ttgaaatcaa	aagaatctga	catcatgaca	acaaatgggtg	taattcatgt	tgtagataaaa	240
ctcctctatc	cagcagacac	acctgttggg	aatgatcaac	tgctggaaat	acttaataaaa	300
ttaatcaaat	acatccaaat	taagtgtgtt	cgtggtagca	ccttcaaaga	aatccccgtg	360
actgtctata	gacccacact	aacaaaagtc	aaaattgaag	gtgaacctga	attcagactg	420
attaaagaag	gtgaaacaat	aactgaagtg	atccatggag	agccaattat	taaaaaatac	480
acaaaaatca	ttgatggagt	gcctgtggaa	ataactgaaa			520

<210> 103
 <211> 479
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(479)
 <223> n = A,T,C or G

<400> 103						
ctgattctca	ggctagaagt	gtcacttttc	ttatctgtac	ttccaaagca	ctttcgtata	60
tttttattat	ggcattttata	tatagttcat	ttatatattaa	attttaattc	catgaacaat	120
caagtaccaa	gtataatgga	gaagggtgctc	atcctctgcc	ttccttgagc	ttctgggtga	180
tgccaggccc	aagtctttgt	ggcaccagc	tccatgcttt	gaatactatg	tggctgaatg	240
aatttttaaa	atctcaaagc	agttaaacag	caggaaagcc	cattaacttc	gtactgaaaa	300
agcaacatac	tgtgatgata	cgggatgaca	tcatttcagg	ttgggcatac	aaaaaagtaa	360
ggaagctaaa	ctaagactat	actcaccagg	ccatttagaa	gttttaataa	atgcctccac	420
tatttttttt	cttanacata	gcttttaagt	gggaaatgga	attagtaaat	gactattttt	479

<210> 104
 <211> 324
 <212> DNA
 <213> Homo sapien

<400> 104						
tgaccatcca	tatccaatgt	tctcatttaa	acattaccca	gcacatttgt	ttataatcag	60
aaactctggt	ccttctgtct	ggtggcactt	agagtctttt	gtgccataat	gcagcagtat	120
ggagggagga	ttttatggag	aaatggggat	agtcttcatg	accacaaata	aataaaggaa	180
aactaagctg	cattgtgggt	tttgaagggt	ttattatact	tcttaacaat	tctttttttc	240
agggactttt	ctagctgtat	gactgttact	tgaccttctt	tgaaggcat	tcccaaaatg	300
ctctattttt	gatagattaa	catt				324

<210> 105
 <211> 541
 <212> DNA
 <213> Homo sapien

32

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<400> 105
cttggttcca gaacctgacg acccgggcag ggcgacgtct cttttgacta aaagacagtg      60
tccagtgtct cagcctagga gtctacgggg accgcctccc ggcgcgccac catgcccac      120
ttctctggca actggaaaat catccgatcg gaaaacttcg aggaattgct caaagtgtctg      180
ggggtgaatg tgatgctgag gaagattgct gtggctgcag cgtccaagcc agcagtggag      240
atcaaacagg agggagacac tttctacatc aaaacctcca ccaccgtgog caccacagag      300
attaacttca aggttgggga ggagtttgag gaggagactg tggatgggag gccctgtaag      360
agcctggtga aatgggagag tgagaataaa atggtctgtg agcagaagct cctgaaggga      420
gagggcccca agacctcgtg gaccagagaa ctgaccaacg atggggaact gatcctgacc      480
atgacggcgg atgacgttgt gtgcaccagg gtctacgtcc gagagtgagt ggccacaggt      540
a                                                                541

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<210> 106
<211> 391
<212> DNA
<213> Homo sapien

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<400> 106
cagaagtctt ggactgcaac tacatacatg gaatatgaga ctcttaccct gggagatatg      60
attaggagaa gtggtggcca cagtcgaaaa atcccaaggc ccaaacctgc accactgact      120
gctgaaatac agcaaaagat tttgcatttg ccaacatctt gggactggag aaatgttcat      180
ggtatcaatt ttgtcagtcg tggtcgaaac caagcatcct gtggcagctg ctactcattt      240
gcttctatgg gtatgctaga agcgagaatc cgtatactaa ccaacaattc tcagacccca      300
atcctaagcc ctcaggaggt tgtgtcttgt agccagtatg ctcaaggctg tgaaggcggc      360
ttcccatacc ttattgcagg aaagtacgcc c                                                                391

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<210> 107
<211> 462
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(462)
<223> n = A,T,C or G

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<400> 107
cgtgacctca agatngcca ctctgactgg aagagtggag agtactggat tgaccccaac      60
caaggctgca acctggatgc catcaaagtc ttctgcaaca tggagactgg tgagacctgc      120
gtgtacccca ctcagcccag tgtggcccag aagaactggg acatcagcaa gaaccccaag      180
gacaagaggc atgtctggtt cggcgagagc atgaccgatg gattccagtt cgagtatggc      240
ggccagggct ccgacctgc cgatgtggcc atccagctga ccttcctgcg cctgatgtcc      300
accgaggcct ccagagaacat cacctaccac tgcaagaaca gcgtggccta catggaccag      360
cagactgggn acctcaataa ggccctgtc ctccagggtc ccaacganat ngagatccgc      420
gccgagggca acagccgctt cacctacagc gtcactgtcg at                                                                462

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<210> 108
<211> 580
<212> DNA
<213> Homo sapien

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<400> 108
atataccatt taatacattt acactttctt atttaagaag atattgaatg caaaataatt      60
gacatataga actttacaaa catatgtcca aggactctaa attgagactc ttccacatgt      120
acaatctcat catcctgaag cctataatga agaaaaagat ctagaaactg agttgtggag      180
ctgactctaa tcaaattgtga tgattggaat tagaccattt ggcctttgaa ctttcatagg      240
aaaaatgacc caacatttct tagcatgagc tacctcatct ctagaagctg ggatggactt      300
actattcttg tttatatattt agatactgaa aggtgctatg cttctgttat tattccaaga      360
ctggagatag gcagggctaa aaaggtatta ttatttttcc tttaatgatg gtgctaaaat      420

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33

tcttccctata	aaattccctta	aaaataaaaga	tggtttaatc	actaccattg	tgaaaacata	480
actgtttagac	ttcccgtttc	tgaaagaaag	agcatcgttc	caatgcttgt	tcactgttcc	540
tctgtcatac	tgtatctgga	atgctttgta	atacttgcac			580

<210> 109

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(482)

<223> n = A,T,C or G

<400> 109

caggcgtgca	gtttcccggc	tctccgcgcg	gccggggaag	gtcagcgccg	taatggcggt	60
cttggcgctg	ggaccctacc	tgacccatca	gcaaaagggtg	ttgcggcctt	ataagcgggc	120
gctacgccac	ctcgagtcgt	ggtgcgtcca	gagagacaaa	taccgatact	ttgcttggtt	180
gatgagagcc	cggtttgaag	aacataagaa	tgaaaaggat	atggcgaagg	ccaccagct	240
gctgaaggag	gccgaggaag	aattctggta	ccgtcagcat	ccacagccat	acatcttccc	300
tgactctcct	gggggcacct	cctatgagag	atacnattgc	tacaagggtc	cagaatgggtg	360
cttagatgac	tggcatcctt	ctgagaaggc	aatgtatcct	gattactttg	ccaagagaga	420
acagtggaag	aaactgcgga	gggaaagctg	ggaacgagag	gttaagcagc	tgcaggagga	480
aa						482

<210> 110

<211> 286

<212> DNA

<213> Homo sapien

<400> 110

aatcattctg	cactcactgg	gtgcatagca	tggttagagg	ggctagagat	ggacagtcac	60
caactggcgg	atatagcggg	acatatgata	cttagccacc	agggcacaag	cttaccagta	120
gacaatacag	acagagcttt	tggtgagctg	taactgagct	atggaatagc	ttctttgatg	180
tacctctttg	ccttaaattg	cttttttagt	ctaagattgt	agaatgatcc	tttcaaattg	240
taatcttttc	taacagagat	attttaatat	acttgctttc	ttaaaa		286

<210> 111

<211> 465

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(465)

<223> n = A,T,C or G

<400> 111

agctactggt	aagatttgac	agattgtctt	gtctttttcc	agtatatata	ggtatctata	60
tatgtatata	ctgtatatac	ttatatatat	ttattgtatt	aaatatatac	atatgtatat	120
gtatatataa	gtatgtgtat	atatgtatat	atttaataca	attattaaat	tgtattattg	180
tattaaatgt	atacatatat	acacacatat	atatacatat	gcataatatt	aacacagtta	240
aaataacact	aatgtacca	ttttgtttct	ggccttttca	gntaatgtta	tgaagaattt	300
ttctattttg	ttaaaattct	ccaaaaacat	taaactgcat	tatgttctga	gagtagatgt	360
accacaatta	attctaccat	ttctgtattg	ttggccatgt	aggttgttct	taattttctc	420
attattatga	atgcatgtga	caatcattgg	ttttgcctaa	agttg		465

<210> 112

<211> 773

34

<212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(773)
 <223> n = A,T,C or .G

<400> 112
 ttttttttca gttttttgcag ttggtgtggt tagcagatac tttcttagaa taaaattgat 60
 aactcaattt gattttttaa aagttgtttt agtgatttaa aatgttgata tggaaaaata 120
 ttaaacatta tatagatagt aggcaaattc atataccta atgcaatatta gcttgtagca 180
 ttttaaatta aaatctaaat ttcttgatat attgccacat tagttgtaat gtttaataaa 240
 tgggtggttaa agatttattt gtaatttaat ctgtgtactt agttgccatg gacctctctt 300
 ttagcttttc ataaataaat atcctttaat accttacctc ctcccttcaa ttgactgatg 360
 ctgggatagg gtgttctttg gagcttatct tggtaaagaa ggtcagaagt gacatataac 420
 cctattccct aggggccgag ggtgctttcc ttacagagtt gtattttaag tgagtcaact 480
 cctgagccag catctactaa gagaaccttc aaacataatc ataggcattt aaataatttg 540
 aaaaatcaaa ttccttgcac taaaaacatt tatccttang ttcatttctt tataanggtt 600
 ctctttttta aaaaaaggat tggattttat gaaagggaat ggtggctggg tttttcttaa 660
 gcattatgna aagggggagt acccctattt ttctttctcc ccanggaaa tgggtgaagg 720
 gaacctgggc aatgcccatg attgnaaaaa ttccactttc nttgaacaat ggg 773

<210> 113
 <211> 543
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(543)
 <223> n = A,T,C or G

<400> 113
 gtttttctga tttgaaaaat tgtttataat attactataa gatgagatta acaatctttg 60
 taaaaatcag attatgtttt gggcttaaaa aaaaccctag tgttttctac tattagtgtg 120
 ctcaaagtat ttgtgagtga tagtactcaa atgagaattg catttaattt gtacatagtt 180
 aaatcgtctt gttttgaagc acaaagtcag gatgtttctc atcagaattt tctgtttgaa 240
 tagggaaaag tggcattggc catgaggcat cattaataaac ggaaagcaga ggaaaaattg 300
 gaaagctaca gaaaaaagat tcacatgaaa aaccaagctg aagaaaaaag ctgcagaaca 360
 gtttcgaatg cgacttaaaa aattaagcca agatgnaaat gaagctagaa agggagatct 420
 cagaaagaag ccagccgagc ctgtcaaaca actggatgtc cagaaaaata ttcaggttcc 480
 ccaggggaaa gcatgggtac tgggtttgan gcttggaaga nggagactgg aaggaaagaa 540
 tga 543

<210> 114
 <211> 550
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(550)
 <223> n = A,T,C or G

<400> 114
 ggaaagaggt aagcggtaaa ttacatagac tgctggagga agagtgttcc agtggagaga 60
 aacagagcta gtgcaaaggc cctgaggtga gagcatgcct ggtgtgatcc ggggatggca 120
 aggaggccag ggtggtggat gaggagttag caaggaggan agtacgagga taagaagcca 180

35

ncaaggaaaa	atggcagtg	ggcggatcac	ctangggct	agtacgccat	tgtgaagact	240
ttgccttttg	ctcccaantg	gaatgggtac	tcnttgaagg	cttttaancc	caggaanaaa	300
cattgattga	tttanaagtt	taaanggatc	acntttgggt	attgtggcca	acaagacact	360
gcgggaagaa	gcaagaagg	tagaaagcca	gnaaaccaac	tnaggaggct	tttgcagtaa	420
tcctggntga	nanacantgg	tggctcnggt	taaaaagttt	tggaaaaaat	taaaactggt	480
tgatggtttg	tttctgttc	ttgggggcnt	aggcattcca	actccttacc	gaaagggtta	540
ccccntttga						550

<210> 115

<211> 550

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(550)

<223> n = A,T,C or G

<400> 115

caatgtggca	cttaacttan	tgggtacaac	tgtatcacat	catgtgtgaa	tcgtgagacc	60
actcaaactct	ctctctggga	aaacncggct	gtcccccgga	tggctggcag	gtgttggaac	120
ctcggctctcc	cgtccgtctc	tggggcaagg	tgggtttcct	catgtatngc	aagagtctat	180
cgtgcggtgc	ttctctcttg	gcatacagct	cacagctctt	tggcctatac	agtgtggaaa	240
tttatnctcc	ggtgctggag	gtgttaatgg	gaaagagctc	ggttaaatgc	acttctcact	300
tggcccgtgg	gtgatgctct	acatgactga	attcntctct	nacggggact	gacattgtat	360
ctatacacta	natccttcca	ccanagtggc	gttaaggacg	gtgtctggga	tggaanctga	420
cggtacangc	cccanctctc	tgaaatgagt	ccananatga	actacctgca	tacctctcta	480
aatcactctg	gtctggcatg	ntctccgtgc	cgaaacatat	atatgtatgt	ctctccnecat	540
acgaaaaana						550

<210> 116

<211> 463

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(463)

<223> n = A,T,C or G

<400> 116

cacaatgtgg	tactttactt	agttggtaca	actgtatcat	atcatgtggt	gaatcacgtg	60
tgacgtgact	ccgcaactcc	gcaccagact	acactgcacg	taatnacagc	cngcacncca	120
ggtggacaaa	nattgacgca	atgttgtgtc	antgccaccg	tgccacacca	cctgtggagg	180
acgtcagtct	tctcttcccc	caaaacccag	gacctcntg	atctcccagc	cngaggtcct	240
nggttggtgt	gactgagcnc	aaaaccgagg	tcgttcaactg	gtacttgacg	ctggagtcac	300
atccaganaa	agcccgaag	acatcacngc	cttcgtgtgt	cnctctcacg	tctgcacaga	360
cggctaacgc	aggatcattc	angtccacaa	gtccaccccc	tcanaaactc	tcnaacaagg	420
cagccgaaac	acgtttccct	gccctccgga	gaatacanaa	cag		463

<210> 117

<211> 503

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(503)

<223> n = A,T,C or G

36

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<400> 117
nncactnatg tgctacgtta acttagttgt acaactcgat cctatccatg tggatgaattc      60
tctccagcag tacactgang atacanctta ttgttattga cgtgcgctgc gctcactacc      120
gncagccagg gaatgcgcct caggaaccct ggtgcccacc ctggctggca tngccattgt      180
caaggaagag aaacgagntg ccattggagc cctcctactg ccatgagggc ctgaaacaaa      240
ctgtgntatg ctctgcgaag gtctggtgct aagggtccgc tggctcacta tggcacacca      300
ctcngggctg aagttgtggt cctgaaggta ctcancccag tgtggccggg acctggatac      360
gtgcacattg ccgtgtcgca aaaccagcat tgtatgtgca catgtagttt gttccactga      420
atgtcnctgc ggcctcagat ttcagggaga ttgactctca tctcnttgtc ctactaagag      480
agagcacctc acctgaatgt caa                                     503

```

```

<210> 118
<211> 560
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(560)
<223> n = A,T,C or G

```

```

<400> 118
tggggggnna ctaagtgcta cgttacttag ttgtacgact cgatccctatc atgtggtgaa      60
ttctgnagcn tgggtctcatg agcctctctg gtgcgctgtg tgtatnggta cggcgctctc      120
tatcgcttta tctcttctga ctgcacccgg ggccgggggc atcaccggcc aagaccctgc      180
acaatgaaga ctgcaggagc aggcgggtgg ccacacctgg cctggacctg aagaccnaaa      240
ctggagcagg ctcgngccgg aggactgggc accgcctaca ggccacgtca cccacggtgg      300
ctgggnaaac aatgaaaaca agaagaactt ctctacccaa gagagaagtt caaaaccnng      360
aactcactgt cgggaaattg actaaaactg cngaactgaa gaaaacaacn caaagccnnc      420
tnaagcanag aagngaactg agacgaacat catccnccna actaatgaaa agagagacgt      480
tccctgnaga gacnaagaga gagaaaagac cccagacnng cccggactaa gattctaata      540
agagcttggt gtgagagaag                                     560

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<210> 119
<211> 638
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(638)
<223> n = A,T,C or G

```

```

<400> 119
acaaaagtgc tacgttactt agctgtacga ctogtcatat ccatgtggtg aatcatacgc      60
tattttatat acngtngatc aacatgaagg gttngtgtct gatcccgcgc atcaaaacac      120
gtgttacttt gactccccc aaactactcta gtaataccta ctattgacca gaaccttaca      180
ttacataaac agttnccata ttctgtatat atatgtatac tgtattctta ataagtaagc      240
taagaaatgt tattgaaatc ataaggaaaa gaaatgtatt atacactgta tgtattgtct      300
gtantgtact gtctgttaca agatgatcgt ctgatgaatg atgcgctgca ccccaactat      360
gtattacaaa caatcncttt tcattgtgtc tgacttgctt ctgaaatact ccacacncta      420
tngctttata tggctcctgg gtattcaggt tatntatgcc taactgaaaa tcccagaacc      480
tgaagatatg tttctgtgat cncattactg ganaaagaac gcccatcaat actcncngng      540
tttaacggat cccacactga cncgcgcatc acagagtgtg naatttgtnt acacttntca      600
cgtanctagc tttgaataac gctcttcttt ttcttccc                                     638

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<210> 120
<211> 434

```

37

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (434)

<223> n = A,T,C or G

<400> 120

ngnnnggggca	caaaagctgc	tatgtttaac	ttagcttggg	tacgactcgt	tcatatccat	60
gtgnttgant	caccgctcta	ctgccaagca	tcattttggt	tctacgnctc	aanctgtgna	120
aangatgtgg	gttaggggan	tgaagatgca	aacncctagg	gtangggcat	ttanaactga	180
aaagganagg	aaganaagac	ctgcgaacgt	gggggataag	actanaagaa	agacgggaga	240
naatantgtc	tttgancctc	aaatggaaca	tntcccatcc	tatctgttan	aaancaccan	300
gtaaaatggg	atgtntgcac	naaagaataa	gttaaactaa	acnccggacn	gtgactanaa	360
aatgaangac	cacanatgaa	aaggcgatga	ctngcctggt	tacctancct	gtanacctat	420
attttcnggg	ttat					434

<210> 121

<211> 631

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (631)

<223> n = A,T,C or G

<400> 121

caaagcgcta	tggttaatgag	cttgtagcac	tcgtcatatc	ttgtggtgta	tcatattctc	60
tctctctttc	aacaaactcc	ccagctccac	ccgggctcta	cctccgagac	cagganccaa	120
aacganccaa	gatggctgct	ctgcgcgcc	cgccgcgcc	ctcccgtgc	ccccggcccc	180
gattccttgg	ataaaganaa	gaatcgcaag	aaaccatcaa	tgcactctc	cttctccggc	240
gctcgnctgt	ccggctccgg	gtcggatgct	gcaaatgctg	ggatgccgag	ntgtgcgcgg	300
gcccagntgc	gcacggttac	acacaccact	ctggactgga	gaagaatcat	ttatanttct	360
gtgccgcacc	cgcgtaaat	gcgcttctg	aactcacgaa	agnagtcaat	ntgttctaac	420
gngctgaaca	cacgcagacc	ncacnaaagc	gccgatggga	ctgctgccgg	aacctggaga	480
ctctcaactc	caagaaccgc	gcaaccgggc	ggcctccgct	ccggcgntgg	gaactgtntc	540
ccccgaagt	tggtccggnt	taacgcgacc	cggttanctt	cgtnaaaggg	ngggcctnaa	600
ttcgggtgct	tncnggcggg	gggtgaccgc	c			631

<210> 122

<211> 678

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (678)

<223> n = A,T,C or G

<400> 122

caaagcggct	angttaatta	gctggtagca	ctcgtcatat	catgtggtgn	atccacacat	60
ggaatgaggg	tcccgtcac	tctggggctc	tgctgctctg	gtccatgtgc	cagatntaaa	120
tccagatgac	cagtctcctc	ctccctgtct	gcacgggtgg	ganacgaatc	accatcactt	180
gncgggcaat	caganattan	aaatgattaa	cctggatatca	gcagaaacca	gggaaaccct	240
aagctctgat	ctttgctgca	tcagttacaa	gtggggtoct	tncgcgttca	cggcagtgnt	300
ctggcacaga	ttcatctcac	atcncagctg	cagcctgaaa	aatttacact	tatactgtct	360
acggataaca	ataccctgna	cttcggcaag	gactanggtg	gaatnaaacn	aatgtggctg	420

38

cacatctgtc	ttctcttccc	gctctgataa	cagtnaaatc	tgaactgctc	tgttggtgtgc	480
tgctgatact	tctatccana	aaagccaagt	acatggaagt	gaatacgctt	ccaatcggtt	540
atccagaaat	gtccaaanag	gaacaggacg	nctacgctcg	cacnctgac	ctaaccancn	600
aatcnaaaac	caatctnccc	gcaatccctc	gggctgaccc	ctccaaaact	ccngggaatt	660
taaggaaatc	cccccccc					678

<210> 123

<211> 445

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(445)

<223> n = A,T,C or G

<400> 123

gaggggggng	caaaagcgct	acttaattag	ctgtacgact	cgtcatatca	tgtggtggat	60
cagcatccag	atggcataat	cggctaattgt	cctgggggttc	agatgtatgc	gatgtccggc	120
taatgtgaca	tcttgccanc	tagcttaagg	anggctggct	agaagacatt	gcagaaacag	180
gagctcggcc	cacangtttc	ccaaggctct	caccccatte	catctccagg	gaagctcgcc	240
cagtggcact	gaatggcctc	ctcagcggag	ggtttgggaat	caggctgggc	aagaactgct	300
aatcttgccg	ggactggaac	cagctctccg	gccttctctg	gctccttggg	tctggtgggg	360
aagggaagag	ggaaaagaaa	ggaaatctcc	nggcananga	ngggacaccc	canacaccga	420
agacacnccc	ccctcctgta	actgt				445

<210> 124

<211> 641

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(641)

<223> n = A,T,C or G

<400> 124

gagggggggg	ncaaagcgct	acgttaatta	gctgtacgac	tcgtcatatc	atgtggtgga	60
tcccactaca	angttgtcac	tatatattan	atctatagtn	gagtongtnt	tcccatcccc	120
tgtaaacgaa	tttactattg	ttggggtagt	gtccctactt	tcctgattaa	ggatctgtgc	180
tggggaacaa	gcnttgcata	ccttatatgt	agttaanatt	tattaacata	tcctcatgan	240
ctcattcaca	ctgnanctct	cctnaaaatn	gtgtgctcct	gttacattan	aactaatctg	300
aaataaagac	tctcnaatgc	tgtgcaacat	anttactgtn	tgaaggagca	gtgtnaattg	360
agtaccaatt	tagcatcgat	ttgaaacgca	ccttatttga	actgtgaata	aacactttct	420
gcgtatacta	ctgcttacat	ccaattcngt	gatttaagat	actcgtggta	tagatacact	480
gattgaagtc	cgatatatgc	aaaactcctt	cataggattg	acatgctgat	ntnagtgnnc	540
nttcaatgtg	gagtatactt	acntaattgc	taacgtataa	agtattgaan	gttnaatagt	600
cagcttcngt	gnaaaatnng	aaattagtat	ggtncngttc	c		641

<210> 125

<211> 285

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(285)

<223> n = A,T,C or G

39

<400> 125
 aggggngcac aaagcgctac gttaatnagc tgtacgaccg tccatatcag gtggtggatc 60
 catatgtccg gtattctctg atgtcangct tattataata gtaccaaccc ttcattctctg 120
 aaatgtctgg ttctggttcc ctattatata ccagcactga aaatattcgt atcttagnan 180
 caaaagcatt taaaaagagt taaaaattta ntcactacta tgcacttcaa ggggagaagc 240
 tncactgcnt ncttgagnct angcaagatg cnagcncct ggaag 285

<210> 126
 <211> 282
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(282)
 <223> n = A,T,C or G

<400> 126
 agggmntgac aaagcggcta cggttaatnag ctggtacgac cgtcatatcn tgtggtggat 60
 ccngaacang tagcctcata atcacaacat ccattagcca cagtaaactg attctgtaac 120
 tccactggca atgctgattg gtaatggctg cataaaaccca gtgtatcaat ttantttcgg 180
 ttttgagaca aaatctcata ttatacnctg acatctcnaa cttcgataca tgaccaaata 240
 cgggnagaca ttattcaaan atattttacct tacanaaaaa aa 282

<210> 127
 <211> 634
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(634)
 <223> n = A,T,C or G

<400> 127
 acaaagcggc tacgtttantc agctggtagc accgtccata tcatgtggtg gatcntgaaa 60
 anctttgatc ggctgcggtg gaaacgttgt cngggccggc aagaagagcc gctgtnacaa 120
 tgggtgtcatg agttcagccg aacgcangac gggtctcaca cccgtgctgc ggtgttgcca 180
 tgtccgcacg ggacaatatc ctgggggaccg gtactggtag taactatgat gcattntgct 240
 gantgtgaat gatctcaact catgccagct gtcacattca tagaattctc gtaatatatc 300
 ntcgaaaaat ggtaanatgc tgtgtctttt gccgtcctgt tctatgttta tatcagtcag 360
 ctgttatgac attctatcag tgggttggtg atccatctct gttacnactt tgactcgtct 420
 cattgccgtt gctatagtcc tcaactattgc cagatcaaaa tactgatcac tactaattcc 480
 nacaananac tctggctgga ccactgccc ngtcatgtctg tgtcttgcta tcacatttaa 540
 gctactatta ctgtgttgga atgcataatc tcacaacnaa gtgcgaaatg ngtttccgcc 600
 ttgaatacnc cctactttgc ccctataaag gcgg 634

<210> 128
 <211> 180
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(180)
 <223> n = A,T,C or G

<400> 128
 caaagcgcta cggttaatnag ctgtacgacc gtccatngtc aggtggtgga tccctgttat 60

40

gtcaagaaaa	gtaaatcgtc	tcttcaataa	ggcctttatt	tgggacaggt	ttatttcctg	120
atatnatntc	ttttatactc	ttttctctca	gaaanaaaaa	agtngtntnc	tcttattgtc	180

<210> 129
 <211> 567
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(567)
 <223> n = A,T,C or G

<400> 129	
acaaagcgct	atgttaactt agctgtacga ccgtccatng tcaggtgggtg gatcctcccg 60
tgtgctggat	tcataatgga tctattttaga cagttgagaa taaattattc tattacaata 120
atagatgcta	atatatatat tatgctgttt ggatatctaa atatttgctc acatccttaa 180
tatattttta	aaattctaac aatagtactg ttganataaa gttgagccat attganacnc 240
toccanattg	gtcctagaaa gttacactgg ttgtctctcc ttatgtcctg ttatccaccc 300
tgacgctgcc	gctttatatt cttaatgant tggacggaca gtggatatcog atcgttttga 360
cgacgttaca	ntactnacca tctatacgtc tacttaattg acagcagatt tcgtagcnet 420
cattaggatc	tgttccaacn gttggcaaat naccncggan gaagttccng tagttgtcnn 480
ctccccctat	tgaaacttat gaccnatctt cctttacnca catatcgacc ttcctgacaa 540
cnccttttnn	aaagaactct tcnccca 567

<210> 130
 <211> 557
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(557)
 <223> n = A,T,C or G

<400> 130	
agggnntcac	aaaagcgcta cgtaaantag ctgtacgact cgatcatatca tgtgggtggat 60
cccgcggcgt	goggactgga tgtcaaactc tgcctgcggc gatgcgcgga tcggcgcccg 120
ggatacgttg	caagcgcggg cccggcgcca gccgcactct ccancctgg cgtggccacc 180
cggccaagca	gaatgggtcc tgcagctgcn gtctagcngt ctgcaccaac acgggtgggtg 240
gtgcagcnaa	gtctccggaa tccncaaggt ctattnaatt ctgtgggaaa ttanatctca 300
actcaatagg	cctttccaaa gaactattgc atgatattca acaagtaatt tcttatttca 360
atacactcog	tatcagaatc atgttctttc tcgatctctt ccatcctcog aacagcctgc 420
antgactggt	tcacctagac aannaatata tccttggtat tgggactcag cataactgtc 480
aaatatgcta	tonactcna tcnaagaaat ctttcogaag ctgtatttga ttcattaatt 540
tatccacatt	actggat 557

<210> 131
 <211> 655
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(655)
 <223> n = A,T,C or G

<400> 131	
aggngggcac	aaagcgctat gttactgagc tgtacgnctc gtccattgtc ntgtgggtgga 60

41

tcntcggatn	aggtctgata	tacttcctgt	gngatcnaga	tgnatctncg	tagntcccc	120
cgttggatgc	tgctcatnac	tgctgcattt	ccacgatcca	ccctgtnatg	gctatcctgc	180
tatacacaac	ngcatgatnn	gatatggaa	cctccacaat	ggaagtgttc	tgttatgacc	240
caccacctta	tatncngccg	ctgtctgaaa	ctcaaaccct	ttgcctgtnt	caganacacga	300
tcngttatgt	tactgatgaa	gaaatggaa	actcccaaaa	acagtgtctn	gccgcaaatac	360
ctacttceng	caaactnact	gcgtctotta	atcctaactc	ctctccatan	aanctacagt	420
tactccgtga	agccntgaag	gaaatgggan	agttatagga	aactntcatc	gttataagcc	480
anaatgcntg	attaaataaa	tcgtctttng	tgataaacctc	atcttcactc	ngttatacct	540
atcgttactn	canaancctt	attgaanttg	aattgtnttg	aaactgccga	aaaaaacgtt	600
cttatgtttc	ccggaccttg	ggggatcaat	aatccaatag	cntactcttc	ncgcc	655

<210> 132

<211> 566

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(566)

<223> n = A,T,C or G

<400> 132

agggtnnac	aaagcgctat	gttacttagc	tgtaoctgtc	gtcattntca	tgtgggtggat	60
tcgagcatca	cagctctacg	tgtgtcagct	ctcacgtctg	caccagacgc	tgaagcaaga	120
gtacagtga	agtctccaca	agcctcccag	ccccatcgag	aaacatctcc	aaagccaaag	180
ggcgcccnaa	aaccacngtg	tacacctgcc	ccatcccggg	agaaatgacc	agaacaagtc	240
gctgacctgc	tggtcaagct	ctatccagca	ctccctggaa	tgggaaacat	ggcanccgaa	300
acactacana	cacnctcccg	tgctggatcg	acgtctctcc	tctatgcanc	tcacgtggac	360
aaacagttgc	acagggaaact	ctctctgtcg	tgatgtctgan	ggtctgccaa	cactacccaa	420
aaanctctcc	tgttcccggg	tataatgcga	aggcggcanc	ccnctcccg	gntctcgcg	480
tccacaagat	gntgcacntn	cccgtctatt	cttccagcac	ccanctggaa	ataagcnccn	540
ccatgnccctg	ggccctgaaa	aaaaaa				566

<210> 133

<211> 816

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(816)

<223> n = A,T,C or G

<400> 133

agctngggct	nagcgtataa	aacttaagct	tgggtnaccg	agctcgggat	ccactcagtc	60
cagtngtggg	tgggnaattc	ctngnagcca	ccctnacagc	cagtaagnag	atatngtagg	120
gtaaatgtgt	aagggnaggt	cagcacttac	attaaagtaa	aattgggctc	acaaaccccg	180
nacacagtna	gcattttgtg	gccaattttc	gggttgagg	tgggtgaaca	aacattgctg	240
ggaagccaag	tngctnaaca	ttgccttggg	ttcaaggggg	natgggnaaa	gtcaccggtt	300
aaggggatgg	gcaattgcc	gtgggaaaac	caccgcttgc	ttgaaggctc	tgggacttgc	360
atccttacca	cccaaactcc	gtccaacttg	gacaaaagcc	ttggccgcct	tgccctctcca	420
ggaatgtctt	acaaaatttg	ggtgggttat	tggggttactg	gttccttgtt	gggcccgaa	480
ttgggaaaaa	cttgggtgtg	tctcaaaaac	cggtgtattg	ggttggttca	ccttttggct	540
cccagnttca	aacgtttaca	aacggggaaa	gtnaaaaatc	ttgttcgaaa	aattgccacc	600
cattgnaaaa	gcttttggaa	nttgaaaaac	tcttccttgg	gggggacaaa	ttgtttgggg	660
gctttccaat	tgntcaaaaa	aattgttgtt	cttggttcaaa	agggatgttt	nccgttccgt	720
ggggccaaac	cgttttgctt	gggttgaaca	gccccaaaaa	tttgnancc	ccaccaant	780
tggggaaagc	caagcmttg	ggtttcactg	gcttcc			816

42

<210> 134
 <211> 451
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(451)
 <223> n = A,T,C or G

<400> 134
 tttnangag aggggtcacct gggcagccct gacttttgtc ccctggcaaa gggaccttca 60
 gtgaaccttgg ccttaggaga gcctctgagc acgtcagcca tgtogaaccg ctcaggaagg 120
 gcagcaagaa tttggcttct gacctctgcc tctcctactc gccatctgca ctgggtgtgg 180
 ttgtgcccatt tttacagatg aggaggctgg ggcacgacc agctgaatgc cttgtcccag 240
 gtactgcgta agcagagctg gcagttgaac cccgtgtcct gggtgtcgtt ggggggtgggc 300
 tgcacctga cttgtgaggg cagnagcaag gnttgcacgt gacttcgtga ccgtcaccca 360
 gctctgcagc acatcccgtg acccancctca tccaggccgn atgcaaacct gttgccaggg 420
 ganaaaacca agtcaccgca canctgtggg t 451

<210> 135
 <211> 658
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(658)
 <223> n = A,T,C or G

<400> 135
 gtgggtatctg ccttcccagg aggcaggagt gggggccccc actgatgagc tcatgggtgca 60
 ctotttagctt ttaagacttg tcatacaggg tgcaataaaa caaatgtgc cactcaaat 120
 gtactttttt ggtatatatt gatcttgctg ttaagagggg ctacaattca gagaggctgc 180
 agacacagaa atagccctga aaagctttct tctctggcag agatttgcaa gtgctgagga 240
 aatacacgtt agtgaagtga acagaggaga aaagcatttc tctgaggcac accccacccc 300
 caocttatct gcctaattgg atcaaggaaa gattaactcc caggaaaaac agactgagat 360
 cctaattgctt taaagggtctg actgagaaac ttctccatag gccactgtct atcttcctga 420
 gggcancctt ggggagcccc tgagagactc acatcttgtg tggggacagc cttgggtcac 480
 caagcatacc tctctctctt cccattacc tgaaaccac ctccnnaaaa cccagcccc 540
 tattctctct gttagcctcag gatgtgaaga aatcttcac attgggcctc ttggagctca 600
 tatttgctgc tcntgtnttg tatatnaatt attgcattta tggtaatat cctttgcc 658

<210> 136
 <211> 478
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(478)
 <223> n = A,T,C or G

<400> 136
 gaagtctcgc gagtataaga acagtaacca gctccgggag taccagctgg aagggatgaa 60
 ctggcttctt ttttaactgg ataacagaaa aaactgtatt ttggctgatg agatgggcct 120
 agggaaaaacc atccagtcca tcacattcct ttcagaaata tttctgagag gaatccacgg 180
 cccttttctc attatcgccc ctctctccac catcactaac tgggagcggg agttccggac 240
 atggacagag atgaatgcca ttgtgtacca cggcagccag atcagcaggc agatgatcca 300

43

gcagtatgaa	atggtgtaca	gagacgcccc	gggaacccct	ttcaggagtc	ttcaagttcc	360
acgtcgtcat	cacaacnttt	gaatgatcct	agcagactgc	ccagagttga	agaagaattc	420
actggaactg	tgtggataat	tggatgaaac	ccccagact	ggaagaatan	ggaactgc	478

<210> 137

<211> 612

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(612)

<223> n = A,T,C or G

<400> 137

gcaggggctc	ttgcaaatta	acacaaaata	ataattaaaa	atgaaacgaa	attgaggata	60
ttcttagaaa	gggtgaagga	catgaaatac	attactatct	gggatttcaa	cctttccaaa	120
ggtcaataaa	tccccaaata	aaatgtaaat	ccaaggctac	ctgagaattc	catttctggt	180
gcatctttgt	tcatgatgag	catatgtctt	ttcattttga	ggacttttta	aaagagaaga	240
gtgacacaca	atgcaacatg	gacaaggaat	gaaaattgct	ttagacactg	cactttgaac	300
atacaaacct	gggaggtgcc	agggctctgac	actgtatatt	tcttcctttg	atctgattct	360
tccaaacagg	atccatgtac	tggcaaat	ccctagtgtt	ccctggtaag	catcaaagta	420
aaccactggt	tggcctcggt	atttctacat	tggctttctc	cattgntttt	atacataaaa	480
aaaaaanaaa	gaaagaaaac	tcactgggca	ttttacatgg	ggtttccata	ttggtcctta	540
atcattcagt	ttgaaagtaa	atcaaagagg	aatgaanagt	taaagngctt	tgaaattggg	600
gtgaaaactt	ca					612

<210> 138

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(478)

<223> n = A,T,C or G

<400> 138

gcaggggctc	ttgcaaatta	acacaaaata	ataattaaaa	atgaaacgaa	attgaggata	60
ttcttagaaa	gggtgaagga	catgaaatac	attactatct	gggatttcaa	cctttccaaa	120
ggtcaataaa	tccccaaata	aaatgtaaat	ccaaggctac	ctgagaattc	catttctggt	180
gcatctttgt	tcatgatgag	catatgtctt	ttcattttga	ggacttttta	aaagagaaga	240
gtgacacaca	atgcaacatg	gacaaggaat	gaaaattgct	ttagacactg	cactttgaac	300
atacaaacct	gggaggtgcc	agggctctgac	actgtatatt	tcttcctttg	atctgattct	360
tccaaacagg	atccatgtac	tggcaaat	ccctagtgtt	ccctggtaag	catcaaagta	420
aaccactggn	tggcctcggt	atttctacat	tggctttctc	cattggtttt	atacataa	478

<210> 139

<211> 597

<212> DNA

<213> Homo sapien

<400> 139

gttatttgggt	agtttttagag	atgaggaact	aaggaccag	ttgctcagtg	tttcctagct	60
agtgaataga	gactagacac	caagtgttct	acgtgcagac	tttatactgc	tcagcctggc	120
acacaaaatg	gcaatggcat	agtccccaga	ctgtgggtccc	aactgtctct	ttcctaacag	180
ctccccaggc	acccacactt	ttctgcctct	ttttcaatct	gtacccttga	ccctcctcct	240
ttttctgctt	tgtcagactc	cttaaggcac	ttcataaatt	aaccatttcc	agggatttcc	300
cctcacacat	gagttattcc	agtggacagg	gcagcctcat	gggtgcctgt	ggagggtgaa	360

44

gggtctgcct	ggccgtaggt	gtgatcacac	actcccgttg	taaccocctgc	ctcctgtgac	420
acttgctgcc	ccacgattta	gctgctttgt	gttccgtgcc	tcctgtttgc	tggtgaactc	480
ctgagttggg	gggcgctcatt	ccctccactg	tagttcttcc	gcgatgctga	atccacccac	540
ggtcagcacc	actcggaat	acttcacagt	cctgtagagg	aagacaggtc	caggttt	597

<210> 140

<211> 368

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (368)

<223> n = A,T,C or G

<400> 140

tttacatcta	gactccacag	acagaaacgt	ttcattttta	ttgagttaat	tttgaaatat	60
atgaatccct	gaccatttgt	tatcactagc	tgttactcta	tcaggacagt	tgctgaagtt	120
ttttgtcact	aaatttaaaa	atcaactatc	aggttgtccc	ttggatgacc	tgagatttct	180
agagacaaaa	gaaatctatt	cttcctgatt	gaagaaagag	tctgagattt	tttttaaacc	240
actgatttgg	ggatcagggt	gtagccagtg	tctcaaaactc	tcocctgtcc	cttttttggt	300
ttgctcaagg	agtgggctnt	gaggnctcaa	gaattggggg	ngttactggg	ttatttttga	360
ttaggggg						368

<210> 141

<211> 674

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (674)

<223> n = A,T,C or G

<400> 141

aatgtcaatc	tttgctcggt	cagtgaggat	gtcgccgtgt	gagggaaaaa	tagtagctgt	60
tgccatattc	ctttaactcc	ccccccccgc	cccccgcaat	atgtcccctg	aataaacttt	120
gtgggtagtt	tttcttcatt	cccagaactg	ttatgaggta	agttcagaaa	ttgccagctt	180
cctgatgctc	tatgctttga	acacacaaaa	taatcaaagg	tgctctttag	taggatcctt	240
tccttatcaa	aataacagta	acaccaatc	tgaggcctca	agcccactcc	ttgagcaaaa	300
caaaaaagg	acaggggaga	gtttgagaca	ctggctacac	cctgatcccc	aaatcagtg	360
tttaaaaaaa	atctcagact	ctttcttcaa	tcaggaagaa	tagatttctt	ttgtctctag	420
aaatctcagg	tcattccaagg	gacaacctga	tagttgattt	ttaaatttag	tgacaaaaaa	480
actttcagca	actgtcctga	taggagtaac	caggctagnt	ggataaccaa	atggggtnca	540
agggggaatn	tcataatatt	ttcaaaaaat	taaaccttca	attaaaaaaa	tggaaaaacc	600
ggttttcntg	gtcctgggtg	ggaggttctt	aagnatggta	aaaaaaggaa	atttccccac	660
ccaacnacct	tggg					674

<210> 142

<211> 669

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (669)

<223> n = A,T,C or G

<400> 142

45

gttggaact	tantcctcaa	tgcaatagtg	ttgagatgtg	ggaccttta	gtgataatta	60
gatcatgagg	gatttgcctc	attcattaat	tatttgctatt	atctcaggtg	agttagttat	120
cggagattga	aatcctgata	aaaagttgag	tttggtctct	ctgtctctct	ctctctctcc	180
actctagaat	tgtaaaaaac	taatctctat	tctgcataaa	ttaccagtc	tcaggtattc	240
cattatatta	gcaggaaatg	gactaagaca	ctactttata	aaattttgca	gtttccaatg	300
ttcagctttt	ccttgatccg	gcttcatcta	catttttctt	tgcttggtac	tgatggtgaa	360
atcttctgt	tgcttttcat	ttatggctta	cactatcaca	tgctctctat	taattcatgc	420
cttctatttc	cttctgttgt	tttggaagc	atctcttttc	atgggctcat	tttagctctg	480
taagacatat	cgaaaactca	cttgattcct	cctgcatgca	tagagctctg	ctggggaagt	540
ctccttctgc	atgctacgcc	ttcccaccaa	agacaaggct	ttgcttattt	gcncattctg	600
tttaacgtct	gccaaatatg	nggtcttgac	ncataagaaa	actggtttga	nccgcaaaan	660
aaaattttg						669

<210> 143
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 143						
agaccttatt	tggtaatctg	ctgtcttcca	gtgtctctgc	attagatacc	attactacag	60
tagcacttgg	atctctcaca	tctattccag	aaaatgtgtc	tactcatggt	tctcagattt	120
ttaatatgat	actaaaagaa	caatcattag	cagcagaaag	taaaactgta	ctacaggaat	180
tgattaatgt	actcaagact	gatcttctaa	gttcaactgga	aatgatttta	tccccaaactg	240
tggtgtctat	actgaaaatc	aatagtcaac	taaagcatat	tttcaagact	tcattgacag	300
tgcccgataa	gatagaagat	caaaaaaagg	aactagatgg	ctttctcagt	atactgtgta	360
acaatctaca	tgaactacaa	gaaaatccat	ttgttccttg	gttgagtcac	aaaagcaatg	420
tggaaccta	actgaagacc	tgaagacaat	aaagcagacc	cattcccagg	aactttgcaa	480
gttaatgaat	ctttggacag	a				501

<210> 144
 <211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G

<400> 144						
gatatctcag	cacctgactt	acacatctta	catcctcaag	caaactcccc	agggcacatt	60
tttagttggc	cagccatcac	cccagacttc	tggaaaacaa	ctcaccactg	ggtcagtggt	120
ccaaggaaca	ctgggagtca	gcacatcttc	tgacacaagg	caacaaacgc	taaaagtcac	180
ctctggacag	aaaaccacat	tgtttacaca	ggcagcccat	ggaggacagg	catctctaata	240
gaaaatatcc	gatagcacgt	tgaagactgt	gccagccacc	tcacagctct	cgaagcctgg	300
aaccacaatg	ctgagagtag	caggaggggt	tatcacaact	gccacttccc	ctgccgtggc	360
cctctcagca	aacggctcct	gccaacagtc	tgaaggaatg	gctnccgtgt	cttcatctac	420
ggncaaagtt	tgtaacgaaa	acttctgggc	agcaacaaag	tgtgtgtgan	ccaagccacc	480
cgtggggaac	cttgcaagg	t				501

<210> 145
 <211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G


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<400> 145
ggaatccgag ccggctaccc cctctccgag cgccagcagg tggcccttct catgcagatg      60
acggccgagg agtctgccaa gagcccagtg gacacaacac caaagcacc ctcctcagtct      120
acagtgtgtc agaagggaac gcccaactct gcctcaaaaa ccaaagataa agtgaacaag      180
agaaacgagc gtggagagac ccgcctgcac cgagccgcca tccgcgggga cgcccggcgc      240
atcaaagagc tcatcagcga gggggcagac gtcaacgtca aggacttcgc aggttgagc      300
gcgctgcacg aggcctgtaa ccggggctac tacgacgtcg cgaagcaact gctggctgca      360
ggtgcggagg tgaacaccaa gggcctagat gacgacacgc cttttgcacg acgcttgcca      420
acaacgggca ctacaaggtg gtgaaactgc ttgttgoggt acnganggaa cccgnacaaa      480
acaacaggaa aagcgaagac c

```

<210> 146

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

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<400> 146
ggcccggaca cggacaggat tgacagattg atagctcttt ctcgattccg tgggtggtgg      60
tgcatggccg ttcttagttg gtggagcgat ttgtctggtt aattccgata acgaacgaga      120
ctctggcatg ctaactagtt acgcgacccc cgagcggtcg gcgtcccca acttcttaga      180
gggacaagtg gcgttcagcc acccgagatt gagcaataac aggtctgtga tgcccttaga      240
tgtccggggc tgcacggccg ctacactgac ttggtcagcg tgtgcctacc ctacgccggc      300
aggcgcggtt aaccgcgttg accccattcg tgatggggat cggggattgc aattattccc      360
catgaacgan gaattcccag taagtgcggg tcataagctt attccgcact tacctgggga      420
gaagcctttt ggtcttccgg ggacnaaaac agctttgttg ctgaacgcng gcagcaccgg      480
tcgcgccgtc cggtggttac c

```

<210> 147

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

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<400> 147
cagcgccgcc gcccggcccc tccagcttcc cggaccatgg ccaacctgga gcgcaccttc      60
atcgccatca agccggacgg cgtgcagcgc ggcctggtgg gcgagatcat caagcgcttc      120
gagcagaagg gattccgcct cgtggccatg aagttcctcc gggcctctga agaacacctg      180
aagcagcact acattgacct gaaagaccga ccattcttcc ctgggctggt gaagtacatg      240
aactcagggc cggttgnggc catggtctgg gaggggctga acgtggtgaa gacaggccga      300
gtgatgcttg gggagaccaa tccagcagat tcaaagccag gcaccattcg tggggacttc      360
tgcattcagg ttggcaggaa catcattcat ggcagtgatt cagtaaaaag tgctgaaaaa      420
gaaatcagcc tatggtttaa gcctgaagaa ctggttgact acaagtcttt ggctcatgac      480
tggttctatn aataagaagg g

```

<210> 148

<211> 501

<212> DNA

<213> Homo sapien

47

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<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

<400> 148
actcttagct tgtcggggac ggtaaccggg acccggtgtc tgctcctgtc gccttcgcct      60
cctaataccct agccactatg cgtgagtgc tctccatcca cggtggccag gctgggtgtcc      120
agattggcaa tgcctgctgg gagctctact gcctggaaca cggcatccag cccgatggcc      180
agatgccaaag tgacaagacc attggggggag gagatgactc cttcaacacc ttcttcagtg      240
agacggggcgc tggcaagcac gtgccccggg ctgtgtttgt agacttgga cccacagtca      300
ttgatgaagt tgcactggc acctaccgcc agctcttcca ccctgagcag ctcatcacag      360
gcaaggaaag tgctgccaat aactatgcc gagggcacta caccattggc aaggagatca      420
ttgaccttgt gttggaccga attcgcaagc tggctgacag tgcaccggtc ttcaggggctt      480
cttggttttn cacagctttg g                               501

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```

<210> 149
<211> 501
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

<400> 149
cgccccgggca ggaatagaag atgaacaaac ccataacacc atcaacatat gtgcgctgcc      60
tcaatgttgg actaattagg aagctgtcag attttattga tcctcaagaa ggatggaaga      120
agttagctgt agctattaaa aaaccatctg gtgatgatag atacaatcaa gtttcacata      180
aggagatttg aagcattctt caaactggaa aaagtccac ttcttgaata ctgtttgact      240
gggggcacca caaattggac agttggtgat cttgtggatc ttttgatcca aaatgaattt      300
ttgctcctgc gactcttttg ctcccagatg ctgttcccaa actgctaata cactaccttc      360
taaagaagct ataacagttc agcaaaaaa gatgcctttc tgtgacaaag acaggacatt      420
gatgacacct gtgcanaatc ttgaacaaag ctatatgcc cctgactcct caagtccana      480
aaataaaaagt ttaaaaagtta g                               501

```

```

<210> 150
<211> 501
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

<400> 150
cagcacagga tactgatatt ctgtcagctg aaaagcatgc ttgatatagt agagcatgat      60
ctcctcaaac ctcacttgcc ctctgtcaact tatttgagat tagatggcag catacctcct      120
ggtcagaggc attccattgt ttcccggttt aataatgac catctataga cgttctgtta      180
cttaccactc acgttgggtg cctgggactt aatttgacag gcgctgacac agtagtattt      240
gtggagcatg actggaantc tatgcgagat ctacaagcca tggaccgggc ccatcgcat      300
gggcagaaac gtgtggttaa cgtatccgat tgataaccag aggaacattg gaagaaaaaa      360
taatggggtt gcagaaaatt caagatgaac catagcgaat ctgttattag ccaagagaat      420
tcttagtttg canacatggg ggactgatca gctttcttga atctgtttac tcttggataa      480
gggatggcaa aagcagaaaa a                               501

```

```

<210> 151

```

48

<211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G

<400> 151
 atggaggggt gtgtgtctaa cctaattggc tgcaacctgg cctacagccg gaagctggaa 60
 gagttgaagg agagtattct ggccgataaa tncctgnnta ctacaactga ccaggacagc 120
 agaactgcat tgcaactggc atgctcagct ggacatacag aaattgttga atttttgttg 180
 caacttggag tgccagtga tgataaagac gatgcagggt ggtctcctct tcatattgcg 240
 gcttctgctg gccgggatga gattgtaaaa gcccttctgg gaaaagggtgc tcaagtgaat 300
 gctgtcaatc aaaatggctg tactccctta cattatgcag cttcgaaaaa caggcatgag 360
 atcgctgtca tgttactgga aggcggggct aatccagatg ctaaggacca ttatgaggct 420
 acagcaatgc accgggcagc agccaagggt aacttgaaga tgattcatat ccttctgtac 480
 tacaaagcat ccacaaacat c 501

<210> 152
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 152
 gccgcgcgaa gccgcgccag aactgtactc tccgagaggt cgttttcccg tccccgagag 60
 caagttttatt tacaaatggt ggagtaataa agaaggcaga acaaaatgag ctgggctttg 120
 gaagaatgga aagaaggact gcctacaaga gctcttcaga aaattcaaga gcttgaagga 180
 cagcttgaca aactgaagaa ggaaaagcag caaaggcagt ttcagcttga cagtctcgag 240
 gctgcgctgc agaagcaaaa acagaagggt gaaaatgaaa aaaccgaggg tacaaacctg 300
 aaaagggaga atcaaagatt gatggaaata tgtgaaagtc tggagaaaac taagcagaag 360
 atttctcatg aacttcaagt caaggagtca caagtgaatt tccaggaagg acaactgaat 420
 tcaggcaaaa aacaaataga aaaactggaa caggaaacta aaagtgtaaa tctgacttga 480
 aagaagcaac aactggcatc t 501

<210> 153
 <211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G

<400> 153
 agagagagag agagagagag gagcgagaga gtgtgagcga gaaagaataa aaggaaagaa 60
 gattttctct atgtatataa agatggccac gttagcaaac ggacaggctg acaacgcaag 120
 cctcagtagc aacgggctcg gcagcagccc gggcagtgcc gggcacatga acgattaag 180
 ccacagcccg gggaacccgt cgaccattcc catgaaggac cacgatgcca tcaagctgtt 240
 cattgggcag atccccgcga cctggatgag aaggacctca agccccctt cgaggagttt 300
 ggcaaaatct acgagctttac ggttctgaag gacagggtca caggcatgca caaaggctgc 360
 gccttctctc cctactgcga gcgtgagtca gcgctgaagg cccagagcgc gctgcacgag 420
 cagaagactc tgcccgggat gaaccgggcc cgatccnagg tgaagccttg cggacagcga 480
 gaaccgagga gatagaaact c 501

<210> 154
 <211> 501

49

<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

<400> 154
ttccttcctg tgtgaggccg gctgagggca cttgctcttg ctgtttctgc ccctgggtta 60
acattcaaga tggatcatgc tgaagccttt tctcgctcctt tgagtcggaa tgaagttgtt 120
ggtttaattt tccgtttgac aatatttggt gcagtgacat actttactat caaatggatg 180
gtagatgcaa ttgatccaac cagaaaagcaa aaagtagaag ctcagaaaca ggcagaaaaa 240
ctaattgaagc aaattgggag tgaataatgt gaagctctca gaatatgaaa tgagtattgc 300
tgctcatctt gtagaccctc ttaatatgca tggtacttgg agtgatatag caggttttaga 360
tgatgtcatt acggatctga aagacacagt catcttacct atcaaaaaga aacatttgtt 420
tgagaattcc aggtctctgc agcctccaaa aggtgntctt ctctatgggc ctccagctgt 480
ggtaaaacgt tgattgcaa g 501

<210> 155
<211> 601
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(601)
<223> n = A,T,C or G

<400> 155
aggaggagga acagcaggag gaggaactca aagtactgct ggccctggag ggatatctca 60
gcacctgact tacacatctt acatcctcaa gcaaaactccc cagggcacat ttttagttgg 120
ccagccatca cccagactt ctggaaaaca actcaccact gggtcagtgg tccaaggaac 180
actgggagtc agcacatctt ctgcacaagg acaacaaacg ctaaaagtca tctctggaca 240
gaaaaccaca ttgtttacac aggcagccca tggaggacag gcatctctaa tgaaaatata 300
cgatagcacc ttgaagactg tgccagccac ctacacagctc tcgaagcctg gaaccacaat 360
gctgagagta gcaggagggg ttatcacaac tgccacttcc cctgccgtgg ccctctcagc 420
aaaaggctct gcacaacagt ctgaaggaat ggctcccgtg tottcatcta cggtcagttc 480
tgtaacgaaa acttctgggc agcagcaagt gtgtgtgagc caggccaccg tgggaacctg 540
caaggntgcc accccccctg cgtcagcgcc acgtncctcg tgctacacca aaccccatct 600
c 601

<210> 156
<211> 501
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

<400> 156
caagaaagga gaaagagagc tcaaaatcgg agacagagta ttggttggtg gactaaggc 60
tggtgtagtc cggtttcttg gggagaccga ctttgccaag ggggagtggg gtggcgtgga 120
gttagatgag ccacttgga agaattgatg cgctgttgct ggaacaagggt attttcagtg 180
tcaacccaaa tatggcttgt tcgctcctgt ccacaaagt accaagattg gcttcccttc 240
cactacacca gccaaagcca aggccaacgc agtgaggcga gtgatggcga ccacgtccgc 300
cagcctgaag cgcagccctt ctgcctcttc cctcagctcc atgagctcag tggcctcctc 360

50

tgtgagcagc	angcccagtc	ggacaggact	attgactgaa	acctcctccc	gttacgccag	420
gaagatctcc	ggtaccactg	ccctccanga	ggcccttgaa	ggaaaaacan	cagcacattg	480
agcancttgc	tggcnggaac	c				501

<210> 157
 <211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (501)
 <223> n = A,T,C or G

<400> 157						
caccctcttc	gtcgcttcgg	ccagtgtgtc	gggctgggcc	ctgacaagcc	acctgaggag	60
aggctcggag	ccgggccccg	accccgccga	ttgccgccc	cttctctcta	gtctcacgag	120
gggtttcccg	cctcgcaccc	ccacctctgg	acttgccttt	ccttctcttc	tccgogtgtg	180
gagggagcca	gcgcttangg	cggagcgagc	ctggggggcc	cccgcctga	agacatcgcg	240
gggaccgatt	caccatgnag	ggcgccggcg	gngcgaacga	caagaaaaag	ataagtctctg	300
aacgtcgaaa	agaaaagtct	cgagatgcag	ccanactctg	gcgaagtaaa	gaatctgaag	360
ttttttatga	gcttgctcat	cagttgccac	ttccacataa	tgtgagttcg	catcttgata	420
angcctcttg	tgatgaggct	taccatcagc	tatttgctgt	tgaggaaaact	tctggatgct	480
ggtgatttgg	atattgaaga	t				501

<210> 158
 <211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)... (501)
 <223> n = A,T,C or G

<400> 158						
acgggggtcac	ccacacgggtg	cccatctacg	agggctacgc	cctccccccac	gccatcctgc	60
gtctggacct	ggctggcccg	gacctgaccg	actacctcat	gaagatcctc	actgagcgag	120
gctacagctt	caccaccacg	gcgagcgggg	aaatcgtgcg	cgacatcaag	gagaagctgt	180
gctacgtcgc	cctggacttc	gagcaggaga	tggccaccgc	cgcatcctcc	tcttctctgg	240
agaagagcta	cgagctgccc	gatggccagg	tcataccat	tggcaatgag	cggttccggg	300
gtccggaggc	gctgttccag	ccttccttcc	tgggtatgga	atcttgcggn	attcacgana	360
ccaccttcaa	ctccatcatg	aagtgtgacg	tggacatccg	caaagacctg	tacgccaaca	420
ccgtgctgtc	gggcgggnacc	accatgtacc	cgggcattgc	cgacaggatg	caaaaaggag	480
atcacccgcc	cttggcgccc	a				501

<210> 159
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 159						
cgagcgggac	tggctgggtc	ggctgggctg	ctggtgcgag	gagccgcggg	gctgtgctcg	60
gcggccaagg	ggacagcgcg	tgggtggccg	aggatgctgc	ggggcggtag	ctccggcgcc	120
cctagctggt	gactgctgcg	ccgtgctca	cacagcccga	ggcgggctcg	gcgcacagtc	180
gtgctccgc	gcgcgcgccc	ggcgcgctc	caggtgctga	cagcgcgaga	gagcgcggcc	240
ctcaggagca	aggcgaatgt	atgacaacat	gtccacaatg	gtgtacataa	aggaagacaa	300
gttgagagaag	cttacacagg	atgaaattat	ttctaagaca	aagcaagtaa	ttcaggggct	360
ggaagctttg	aagaatgagc	acaattccat	tttaciaaagt	ttgctggaga	cactgaagtg	420

51

tttgaagaaa gatgatgaaa gtaatttggg ggaggagaaa tcaaacaatga tccggaagtc 480
actggagatg ttggagctcg g 501

<210> 160

<211> 487

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(487)

<223> n = A,T,C or G

<400> 160

aagatctcag	tctgactctt	ttggaacaag	tcaaactgcc	catgatgttg	ctgatcagcc	60
aaggcctgga	tcagagggga	gcttctgtgc	atcttcaaac	tctccaatgc	actcccaagg	120
ccagcagttc	tctgggtgtc	cccaacttcc	tggacctgtg	ccacttcagg	agtaactgat	180
acacagaata	ctgtaaatat	ggcccaagca	gatacagaga	aattgagaca	gcggcagaag	240
ttacgtgaaa	tcattctcca	gcagcaacag	cagaagaaga	ttgcaggtcg	acaggagaag	300
gggtcacagg	actcaccgcg	agtgccttca	tccanggcct	ctttaacact	ggcaaccaag	360
agaatggtta	acccaggctt	ttaaccaana	acccccacct	tccttttctt	gggggaacat	420
ttaggtcttc	ctggttggcc	ccttcctttt	anggaacctt	anaatttgct	tggtttttcc	480
ccnaaaa						487

<210> 161

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 161

ggttcccggc	ccagtcccgt	cctgcagcag	tctgcctcct	ctttcaacat	gacagatgcc	60
gctgtgtcct	tcgccaagga	cttcctggca	ggtggagtgg	ccgcagccat	ctccaagacg	120
gcggtagcgc	ccatcgagcg	ggtcaagctg	ctgctgcagg	tgcagcatgc	cagcaagcag	180
atcactgcag	ataagcataa	caaaggcatt	atagactgcg	tggtcctgtat	tccaaggag	240
cagggagttc	tgtccttctg	gcgcggtaac	ctggccaatg	tcatacagata	cttccccacc	300
caggctctta	acttcgcctt	caaagataaa	tacaagcaga	tcttcctggg	tggtgtggac	360
aagagaaccc	agttttggcg	ctactttgca	gggaatctgg	catcggttgg	tgccgcangg	420
gccacatccc	tgtgttttgt	gtaccctctt	gattttgccc	gtaccctgtt	ancantgat	480
gtggggtaaa	agctggagct	g				501

<210> 162

<211> 501

<212> DNA

<213> Homo sapien

<400> 162

gaaaaagaaa	aagaactaca	acggcagaaa	gaaaaggaaa	aagaactaca	aaagatgaaa	60
gaacaagaaa	aggaatgtga	gctggagaag	gaaagggaaa	aattagagga	gaaaattgaa	120
cccagagAAC	ctaattttaga	gcccatggta	gaaaaacaag	aaagtgaaaa	cagctgtaat	180
aaagaggagg	aaccctgttt	cactagacaa	gacagcaatc	gcagtgaaaa	ggaagccaca	240
ccagtgggtg	atgaaacaga	accagaatca	gggtctcaac	ctcgcccggc	tgtattatct	300
ggctattttc	aacagtttca	gaagtcttta	cctccacgat	tccagcggca	gcaggaacag	360
atgaaacagc	agcagtgcca	gcagcagcaa	cagcaagggtg	tacttccaga	ctgttccttc	420
caaccgtcca	gtagtactgt	ccctcctccc	cacacagacc	tcttttcagc	ctatgcagcc	480

52

tctcctcagc atttggttc t 501

<210> 163

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 163

gagctcgacc	agttgcctga	cgagagctct	tcagcaaaag	cccttggtcag	ttttaaagaa	60
ggaagcttat	ctaacacgtg	gaatgaaaag	tacagttctt	tacagaaaac	acctgttttg	120
aaaggcagga	atacaagctc	tgctgtggaa	atgccttttc	agaaattcaa	aacgaagtcg	180
acttttttct	gatgaagatg	ataggcaaat	aaatacaagg	tcacctaaaa	gaaaccagag	240
ggttgcaatg	gttccacaga	aatttacagc	aacaatgtca	acaccagata	agaaagcttc	300
acagaagatt	ggttttcgat	tacgtaatct	gctcaagctt	cctaaagcac	ataaatggtg	360
tatatacgag	tggttctatt	caaatataga	taaaccactt	tttgaagggtg	ataatgactt	420
ttgtgtatgt	ctaaaggaat	cttttcta	ttgaaaacaa	gaaagttaac	aagagtagaa	480
tggggaaaaa	ttcngcggct	t				501

<210> 164

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 164

cgggtgctcg	cccacgaccg	ccagactcga	gcagtctctg	gaacacgctg	cggggctccc	60
gggcctgagc	caggtctgtt	ctccacgcag	gtgttcgcgc	cgccccgttc	agccatgtcg	120
tccggcatcc	atgtagcgct	ggtgactgga	ggcaacaagg	ggcatcggct	tggccatcgt	180
gcgcgacctg	tgccggctgt	tctcggggga	cgtggtgctc	acggcgcggg	acgtgacgcy	240
gggccaggcg	gccgtacagc	agctgcaggc	ggagggocgt	agcccgcgct	tccaccagct	300
ggacatcgac	gatctgcaga	gcattccgcg	cctgcgcgac	ttcctgcgca	aggagtacgg	360
gggcctggac	gtgctggtca	acaacgcggg	catgcgcctc	aagggtgctg	atcccacacc	420
ctttcatatt	caagctgaag	tgacgatgaa	aacaaatttc	tttggtacct	ganatgtgtg	480
cacagaatta	ctccctctaa	t				501

<210> 165

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 165

ccggtgaagg	accgcgaggc	cttcacagag	ctcaacttcc	tgtaccaggt	gagctctgca	60
caagggcccc	acggggacgg	tgctcggcgt	cccagagtga	ctgctccccct	cccgcaggcc	120
gccattgtg	tccttgccca	ggaccccgag	aaccangcgc	tggcgagggt	ttactgctac	180
actgagagga	ccattgcgaa	gcggctcgct	ttgcggcggg	atccctcggt	gaagaggact	240

53

ctctgtcgag	gctgctcttc	cctcctcgtc	ccgggacctca	cctgcaccca	ccgccagaga	300
cgctgcaggg	gacagcgctg	gaccgtacag	acctgcctaa	catgccagcg	cagccaacgc	360
tnnctcaatg	atcccnngca	tttactntgg	ggagacnngn	ctgaggccca	actcggggagc	420
caagcagatt	ccaaaccact	acaacccttg	ccaaacacag	cccactccat	ttcagaccgc	480
cttcctgagg	agaaaatgca	g				501

<210> 166

<211> 412

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(412)

<223> n = A,T,C or G

<400> 166

atgtccaagc	cggtggacca	cgtaagcgg	cccatgaacg	ccttcattggt	gtggctcgcg	60
gctcagcggc	gcaagatggc	ccaggagaac	cccaagatgc	acaactcgga	gatcagcaag	120
cgcttggggc	ccgagtggaa	actgctcaca	gagtcggaga	agcggccggt	catcgacgag	180
gccaagcgtc	tacgcgccat	gcacatgaag	gagcaccocg	actacaagta	ccggccgcgg	240
cgcaagccca	agacgctgct	caagaaggac	aagttcgcct	tcccgggtgcc	ctacggcctg	300
ggcggcgctg	cggacgccga	gcaccctgcg	ctcaaggcgg	gcgccgggct	gcacgcgggg	360
gcgggcggcg	gmctggtgcc	tgagtcgctg	ctcgccaatc	ccgagaaggc	gg	412

<210> 167

<211> 501

<212> DNA

<213> Homo sapien

<400> 167

aaatgcaagt	tgatctggag	aaagaattac	aatctgcttt	taatgagata	acaaaactca	60
cctcccttat	agatggcaaa	gttccaaaag	atttgctctg	taatttgga	ttggaaggaa	120
agattactga	tcttcagaaa	gaactaaata	aagaaagtgt	aagaaaaatg	aagctttgcg	180
ggaagaagtc	attttgcttt	cagaattgaa	atctttacct	tctgaagtag	aaaggctgag	240
gaaagagata	caagacaaat	ctgaagagct	ccatataata	acatcagaaa	aagataaatt	300
gttttctgaa	gtagttcata	aggagagtag	agttcaagg	ttacttgaa	aaattgggaa	360
aaacaaagat	gacctagcaa	ctacacagtc	gaattataaa	agcactgata	aagaattcca	420
aaatttcaaa	acccttcata	tggaactttga	gcaaaagtat	aagatggtcc	ttgaggagaa	480
tgagagaatg	aatcaggaaa	t				501

<210> 168

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 168

ggggcccgcg	gagctcgcg	caggctcctg	ggaaaggacg	gggagtgtta	ccggggagca	60
gctgctccat	tgtgcctcga	ggccccgata	gggctaggcc	gacggcctcc	ctcccttcac	120
ctttcctctc	ctggcggggt	tcggcgggcg	gcgagtgaat	tgccggccacg	cctgaaaggc	180
gactctcctg	attcaagatg	accaacgaag	aacctcttcc	caagaagggt	cgattgagtg	240
aaacagactt	caaagttatg	gcaagagatg	agtttaattct	aagatggaaa	caatatgaag	300
catatgtaca	agcttttgag	ggcaagtaca	cagatcttaa	ctctaattgat	gtaactggcc	360
taagagagtc	tgaagaaaaa	ctaaagcaac	aacagcagga	gtctgcacgc	agggaaaaaca	420

54

tccttgtaat	gcgactagca	accaaggaac	aagagatgca	agagtgtact	acttaaatacc	480
agtacctcaa	gcaagtccan	c				501

<210> 169
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 169						
gctgtgcggc	ggtcccgcgc	ccggcgatgt	tcccgggcac	tccttgagta	gcggcagctt	60
atcccccgcc	cgctagcccg	ccctggtecc	cggtcgctc	gctggctggc	gcggccccgg	120
ccccgctctg	cgctggcccc	gccgcggtgg	aggcgcgcg	gggggacgcg	gccggggatg	180
agcggattgc	gggtgaactc	gccgccgggg	ggccccgcga	agccgtgagc	cgctgctttt	240
ctccgagtcg	ccgccctgcc	cttgatttg	agatcatgtc	catccacatc	gtggcgctgg	300
ggaacgagg	ggacacattc	caccaggaca	accggccgtc	ggggcttata	cgcaattacc	360
tggggagaag	ccctctggtc	tccggggacg	agagcagctt	gttgctgaac	gcggccagca	420
cggtcgcgcg	tccggtgttc	accgagatc	aggccagtgc	gtttgggaat	gtcaaagctg	480
gtggtccacg	actgtcccgt	c				501

<210> 170
 <211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G

<400> 170						
gcacacctt	gccgttcccc	gtgtttgggc	cttgccctgtg	acggtgggaa	aagaaaatgg	60
ccttgctgtg	ctacaaccgg	ggctgcggtc	agcgcttcga	tcctgagacc	aattccgacg	120
atgcttgac	ataccaccca	gggtgtccgg	tcttttcacga	tgcattaaag	ggttggtctt	180
gctgtaagag	aagaacaact	gatttttctg	atttcttaag	cattgtaggc	tgtacaaaag	240
gtagacataa	tagtgagaag	ccacctgagc	cagtcaaacc	tgaagtcaag	actactgaga	300
agaaggagct	atgtgaatta	aaacccaaat	ttcangaaca	catcattcaa	gcccctaagc	360
cagtagaagc	aataaaaaa	ccaagcccag	atgaaccaat	gacaaatttg	gaattaaaaa	420
tatctgcctc	cctaaaacaa	gcacttgata	aacttaaact	gtcatcaggg	aatgaagaaa	480
atnagaaaag	agaagacnat	g				501

<210> 171
 <211> 601
 <212> DNA
 <213> Homo sapien

<400> 171						
agcgacctat	cttgaactcc	acagccttga	tgactttctac	ataggaaagt	attttgagg	60
agtgttgagg	tattttatga	ttcaagcctt	aaatcagaag	acaagtgaag	aaatgaagaa	120
aagaaaaatg	agcaactcct	ttcatggaat	tagaccacct	caacttgaac	aaccagaaaa	180
aatgcctgtc	ttaaaggctg	aagcgtcaca	ttataactct	gacttaaata	acttgctgtt	240
ctgctgccag	tgtgtggacg	tggtatttta	caaccccaat	ttaaagaaag	ttgtagaggc	300
ccacaagatc	gttctctgcg	ctgtaagcca	tgttttcatg	ctgcttttca	atgtgaagag	360
tcccactgac	attcaggatt	ccagtatcat	ccgaactacc	caggatcttt	ttgctataaa	420
cagagatact	gcatttccag	gtgctagcca	tgaatcttca	ggcaaccac	cattacgagt	480
cattgttaaa	gacgccctct	tctgttcttg	tttatcagac	atccttcgct	tcattttattc	540
aggtgctttt	cagtgggaag	aattggaaga	agatatcagg	aagaagtga	aagattctgg	600
g						601

<210> 172

55

<211> 501
 <212> DNA
 <213> Homo sapien

<400> 172
 gaccgttttaa aaaactggta tccagctcac atagaagaca ttgactacga ggaaggaaaa 60
 gtactcatcc atttcaagcg ttggaaccat cgttatgatg agtggttctg ctgggacagt 120
 ccttattttac gccctttaga gaaaatacag ctgaggaaaag agggcttgca tgaagaggat 180
 ggatcttctg aatttcaaataaatgagcag gtccttgctt gctggtctga ttgtcgtttt 240
 taccgggcca aagtcactgc tgttaacaag gatggtactt acactgtgaa attttatgat 300
 ggagtagttc agactgtcaa acatattcat gtcaaagctt tttccaaaga tcagaatatt 360
 gtgggtaatg ctaggcctaa agaaacagat caaaaaagtc tttcatcatc tcctgataaa 420
 cgagagaagt ttaaagaaca gagaaaagca acagtgaatg tgaagaaaga caaagaagat 480
 aaacccttaa agacagaaaa g 501

<210> 173
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 173
 gcgacctatc ttgaactcca cagccttgat gactttctaca taggaaagta ttttggagga 60
 gtgttggagt attttatgat tcaagcctta aatcagaaga caagtgaaaa aatgaagaaa 120
 agaaaaatga gcaactcctt tcatggaatt agaccacctc aacttgaaca accagaaaaa 180
 atgcctgtct taaaggctga agcgtcacat tataactctg acttaaaataa cttgctgttc 240
 tgctgccagt gtgtggacgt ggtattttac aaccccaatt taaagaaagt tgtagaggcc 300
 cacaagatcg ttctctgcgc tgtaagccat gttttcatgc tgcttttcaa tgtgaagagt 360
 cccactgaca ttcaggattc cagtatcatc cgaactaccc aggatctttt tgctataaac 420
 agagatactg catttccagg tgctagccat gaatcttcag gcaaccacc attacgagtc 480
 attgttaaag acgccctctt c 501

<210> 174
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 174
 ccccgagg cgggccgtcg ggcgagccg cgaagatgcc gttggaactg acgcagagcc 60
 gagtgcagaa gatctgggtg cccgtggacc acaggeccctc gttgccaga tcctgtgggc 120
 caaagctgac caactcccc accgtcatcg tcatgggtggg cctccccgcc cggggcaaga 180
 cctacatctc caagaagctg actcgctacc tcaactggat tggcgtcccc acaaaagtgt 240
 tcaacgtcgg ggagtatcgc cgggaggctg tgaagcagta cagctcctac aacttcttcc 300
 gccccgacaa tgagggaagcc atgaaaagtcc ggaagcaatg tgccttagct gccttgagag 360
 atgtcaaaag ctacctggcg aaagaagggg gacaaattgc ggttttcgat gccaccaata 420
 ctactagaga gaggagacac atgaccttc attttgccaa agaaaatgac ttaaggcgt 480
 ttttcatcga gtcggtgtgc g 501

<210> 175
 <211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G

<400> 175
 -ccaacatgac cgaacgaaga agggacgagc tctctgaaga gatcaacaac ttaagagaga 60

56

aggatcatgaa	gcagtcggag	gagaacaaca	acctgcagag	ccaggtgcag	aagctcacag	120
aggagaacac	cacccttcga	gagcaagtgg	aaccaccccc	tgaggatgag	gatgatgaca	180
tcgagctccg	cggtgctgca	gcagctgctg	ccccaccccc	tccaatagag	gaagagtgcc	240
cagaagacct	cccagagaag	ttcgatggca	accagacat	gctggctcct	ttcatggccc	300
agtgccagat	cttcatggaa	aagagcacca	gggattttctc	agttgatcgt	gtccgtgtct	360
gcttcgtgac	aagcatgatg	accggccgtg	ctgccgttgg	gcctcagcaa	agctggagcg	420
ctccactacc	tgatgcacaa	ctacccactt	tcgatgatgga	aatgaagcat	gtctttgaag	480
accctcanag	gcgagagggt	g				501

<210> 176

<211> 378

<212> DNA

<213> Homo sapien

<400> 176

ggcggaagag	gtgattttatt	atatggttgt	tacactcggc	cacaaataaa	cacagaaata	60
gtccagaatg	tcacagggtcc	agggcagagg	accaacatgg	gcatttttgtt	tatgagcaag	120
gtgggtctca	gaggtgatcg	gcgatcagag	ggcgatgaag	ttctagatcc	attgagacaa	180
gctctagaca	gtagcatgca	gtcccacaac	ttgtaccagc	atccccagcg	tctggcatct	240
catgtttctg	ctcctgtggc	ctccacggtg	caacaagcta	gcggtttact	tggacctctg	300
cctcatcttt	cttcttttgc	gcttcagcct	gogcattcgc	ttcttcctcc	acttggctct	360
catggcgag	aggtttcc					378

<210> 177

<211> 501

<212> DNA

<213> Homo sapien

<400> 177

ggcagggagc	tggacctgga	ggcgccgcgc	cgacagcagc	agccatggag	gacgagatgc	60
ccaagactct	atacgtcgtg	aacctttcca	gagatgtgac	agaagctcta	attctgcaac	120
tctttagcca	gattggacct	tgtaaaaact	gcaaaatgat	tatggataca	gctggaaatg	180
atccctattg	ttttgtggag	tttcatgagc	atcgtcatgc	agctgcagca	ttagctgcta	240
tgaatggacg	gaagataatg	ggtaaggaag	tcaaagtga	ttgggcaaca	accctagca	300
gtcaaaagaa	agatacaagc	aatcattttcc	atgtctttgt	tggtgatctc	agcccagaaa	360
ttacaactga	agatataaaa	gctgcttttg	caccatttgg	aagaatatca	gatgcccag	420
tggtaaaaga	catggcaaca	ggaaagtcta	agggatatgg	ctttgtctcc	tttttcaaca	480
aatgggatgc	tgaaaacgcc	a				501

<210> 178

<211> 501

<212> DNA

<213> Homo sapien

<400> 178

agccccgggc	caggccgcgc	ccggggcagg	agcgcagggg	ctttgttatg	cacctaaagc	60
catattggaa	gctccagaag	aaagagcacc	ccccggaagt	cagcagggaa	acgcagagaa	120
ctcctatgaa	ccaccaaaaag	gctgtaaatg	atgaaacatg	caaagctagc	cacataacat	180
caagtgtctt	tccttcagcc	tctctcggta	aagcatcatc	tcgaaagcca	tttgggatcc	240
tttctccaaa	tgttctgtgc	agtatgagtg	ggaagagtcc	tgtagagagc	agcttgaatg	300
ttaaaaccaa	aaagaatgca	ccatctgcaa	cgatccacca	gggcgaagaa	gaaggaccac	360
ttgatatactg	ggctgttgtg	aaacctggaa	ataccaagga	aaaaattgca	ttctttgcat	420
ccaccagtg	tagtaacagg	ataggatcta	tgaaaaataaa	aagttcctgg	gatattgatg	480
ggagagctac	taagagaagg	a				501

<210> 179

<211> 501

<212> DNA

<213> Homo sapien

57

<400> 179
 cgggactagg agcgcgggcg ggccggcgcc agagctgtcc ggctgcgcgg tggcccgggg 60
 ggcccgggcg gcagggcaag cagcgcgcc tcggcctatg cgaccgggtg cgccggcgcg 120
 gcttctgcct ggagaggatt caagatgacc aacgaagaac ctcttcccaa gaagggtcga 180
 ttgagtgaag cagacttcaa agttatggca agagatgagt taattctaag atggaaacaa 240
 tatgaagcat atgtacaagc tttggagggc aagtacacag atcttaactc taatgatgta 300
 actggcctaa gagagtctga agaaaaacta aagcaacaac agcaggagtc tgcacgcagg 360
 gaaaacatcc ttgtaatgcg actagcaacc aaggaacaag agatgcaaga gtgtactact 420
 caaatccagt acctcaagca agtccagcag ccgagcggtt gccaaactgag atcaacaatg 480
 gtagaccagc cgatcaactt t 501

<210> 180

<211> 571

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(571)

<223> n = A,T,C or G

<400> 180
 gagcgtaccg ggTTTTctcc atgctgtttc ttactctcct cttttgcacc cctcccatTT 60
 ccctcgTTTT tctttgaaaa tttctccccc ctccagttcg ctgtccggcc ctcacatgtg 120
 tganaggggc agtgtgccgt taatggccgt gccgggcacc ggccgcctct ggtagtgtg 180
 ggacatgtga agtctgctgg gggcggcggg ttccggcacc tcggcgccgg ggagatacat 240
 gctgatcatg tcccgagggt ccccgccctg gcagggcgcc ctggagtggg aggaagaggt 300
 aaccacaggg gggctggagc tggcctcgga cttgaccacc gaacccatgg agccaanagc 360
 catgccaggg gtgccctgct gcgagtagga catgctgtag gtgggcgagc cgttcatgta 420
 ggtctgcgag ctggtcatgg agttgtactg cagggcgctc acgtcgtaac ggtgcatggg 480
 ctgcatctgc gctgcgccgt gcgcattgag gccgggtgct tgnnggtagc ccaactggtc 540
 ctgcatcatg ctgtactgcc gntgctccac c 571

<210> 181

<211> 501

<212> DNA

<213> Homo sapien

<400> 181
 tgagaccgcc aagatgggtg tgggcgcggt ccctatggcg aagctgctat acttgggcat 60
 ccggcagggtc agcaagccgc ttgccaaccg tattaaggag gccgcccgc gaagcgagtt 120
 cttcaagacc tataatctgcc tcccgccggc tcaactgtat cactgggtgg agatgcggac 180
 caagatgcgc atcatgggct tccggggcac ggtcatcaag ccgctgaacg aggaggcggc 240
 agccgagctg ggcgcagagc tgctgggcga agccaccatc ttcatcgtgg gcggcggctg 300
 cctagtgtg gagtactggc gccaccaggc gcagcagcgc cacaaggagg aggagcagcg 360
 tgctgcctgg aacgcgctgc gggacgaggt gggccacctg gcgctggcgc tggaaagcgt 420
 gcaggcgag gtgcaggcgg gcccgccaca gggcgccctg gaggaactgc gcacagaact 480
 gcaagaggtg cgcgccact c 501

<210> 182

<211> 501

<212> DNA

<213> Homo sapien

<400> 182
 cccagcaga catgtttgcc aaggcctttc gggcacaagtc caacacggcc atcaagggtt 60
 cggacaggag aaagcttcga gctgatgtga caactgcctt cccaccctt ggaactgatc 120
 aagtctctga gttagtacct ggaaaggagg agctcaacat tgtgaagttg tatgctcaca 180

58

aaggggatgc	agtgactgtg	tacgtgagtg	gtggtaaccc	catcctcttt	gaactggaga	240
aaaatctgta	tccaacagtg	tacacgctgt	ggtcctatcc	tgatcttctg	ccaaccttta	300
caacatggcc	tctgggtgctc	gagaaactgg	tagggggagc	agatttgatg	ctgcctggac	360
tggtgatgcc	ccctgctggg	ctgcctcagg	tacagaaggg	cgacctctgt	gccatttctt	420
tggtggggaa	cagagcccct	gtagccattg	gagttgcagc	catgtccaca	gctgagatgc	480
tcacgtcagg	cctgaaggga	a				501

<210> 183
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 183						
atctgctcac	tttagcactc	tggcaattaa	acagaacccc	cttctggcag	aagcttattc	60
gaatttgggg	aatgtgtaca	aggaaagagg	gcagttgcag	gaggcaattg	agcattatcg	120
acatgcattg	cgtctcaaac	ctgatttcat	cgatggttat	attaacctgg	cagccgcctt	180
ggtagcagcg	ggtgacatgg	aaggggcagt	acaagcttac	gtctctgctc	ttcagtacaa	240
tcctgatttg	tactgtgttc	gcagtgcact	ggggaacctg	ctcaaagccc	tggtgcgctt	300
ggaagaagcc	aaggcatggt	atttgaaagc	aattgagacg	caaccgaact	ttgcagtagc	360
ttggagtaat	cttggtctgt	ttttcaatgc	acaaggggaa	atttggcttg	caattcatca	420
ctttgaaaag	ctgtcaccct	tgacccaaac	tttctggatg	cttatatcaa	tttaggaaat	480
gtcttgaaag	agcacgcatt	t				501

<210> 184
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 184						
agttctccca	ggagaaagcc	atgttcagtt	cgagcgccaa	gatcgtgaag	cccaatggcg	60
agaagccgga	cgagttcgag	tccggcatct	cccaggctct	tctggagctg	gagatgaact	120
cggacctcaa	ggctcagctc	agggagctga	atattacggc	agctaaggaa	attgaagttg	180
gtggtggctg	gaaagctatc	ataatctttg	ttcccggttc	tcaactgaaa	tctttccaga	240
aaatccaagt	ccggctagta	cgcgaaattg	agaaaaagtt	cagtggggaag	catgtcgtct	300
ttatcgctca	gaggagaatt	ctgcctaagc	caactcgaaa	aagccgtaca	aaaaataagc	360
aaaagcgtcc	caggagccgt	actctgacag	ctgtgcacga	tgccatcctt	gaggacttgg	420
tcttcccaag	cgaaattgtg	ggcaagagaa	tccgcgtcaa	actagatggc	agccggctca	480
taaaggttca	tttgacaaa	g				501

<210> 185
 <211> 460
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(460)
 <223> n = A,T,C or G

<400> 185						
gcacaaaatg	gcggcggcgg	cggcggcggc	tggtgctgca	gggtcggcag	ctcccgcggc	60
agcggccggc	gccccgggat	ctggggggcg	accctcaggg	tgcagggggg	tgctgatcgg	120
ggacaggctg	tactccgggg	tgctcatcac	cttgaggagaa	tgccctctgc	ctgacgacaa	180
gctccgtttc	acgccgtcca	tgctcagcgg	cctcgacacc	gacacagaga	ccgacctccg	240
cgtgggtggc	tgcgagctca	tccaggcggc	cggtatcctg	ctccgcctgc	cgcaggtggc	300
catggctacc	gggcaggtgt	tgttccagcg	gttcttttat	accaagtcct	tcgtgaagca	360
ctccatggag	catgtgtcaa	tggcctgtgt	ccacctgggt	tccaagatag	aagangcccc	420
aagaccatac	gggacgtcat	caatgtgttt	caccgccttc			460

59

<210> 186
 <211> 401
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(401)
 <223> n = A,T,C or G

<400> 186
 cgtgtttttgg gccggtttctg gagggtgctgg cggcgggggcc tgggtgtcog cccagtgtccc 60
 gaggacgcag gctttggcac cgaagcccgg catcagaggc aaccccgcgg ctccctgccaa 120
 cggtcggggc ccctcgggga ccagcccttc gcggggctgc tgccaaaaaa cctcagtcgg 180
 gaggagctgg ttgatgcgct gcgggcagcc gtggtggacc ggaaaggacc tctagtgcg 240
 ttgaacaagc cacaggttct accagtgcac ggaaaaccag gagagctgac gttgttctca 300
 gtgctgccag agctgagcca gtccctangg ctcagggagc aggagcttca ggttgtccga 360
 ncâctctggga agtaagtggg angggtgaca ggaagctang a 401

<210> 187
 <211> 376
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(376)
 <223> n = A,T,C or G

<400> 187
 gcatccgccc tgtctgggag gtggggggcg cgcctctgnc cagccgccac gtctgggaag 60
 tggggagccc cactgtcccg ctgccacccc gtctgggagg tgtacccaac agctcattga 120
 gaacgggcca tgatgacgat ggcggttttg tcgaatagaa aagggggaaa tgtggggaaa 180
 agaaagagag atcagattgt tactgtgtct gtgtagaaa aagtagacat aggagactcc 240
 attttgttct gtactaagaa aaattcttct tccttgggat gctgttaatc tataacctta 300
 cccccaaccc cgtgtctctc gaaacatatg ctgtgtcaac tcagggttaa atggattaag 360
 ggcggtgcaa gatgtg 376

<210> 188
 <211> 376
 <212> DNA
 <213> Homo sapien

<400> 188
 aacctggagc gcaaccttcat cgccatcaag ccggacggcg tgcagcgcg cctggtgggc 60
 gagatcatca agcgcttoga gcagaaggga ttccgcctcg tggccatgaa gttcctccgg 120
 gcctctgaag aacacctgaa gcagcactac attgacctga aagaccgacc attcttccct 180
 gggctggtga agtacatgaa ctcagggccg gttgtggcca tggctctggga ggggctgaac 240
 gtggtgaaga caggccgagt gatgcttggg gagaccaatc cagcagattc aaagccaggc 300
 accattcgtg gggacttctg cattcaggtt ggcaggaaca tcattcatgg cagtgtattca 360
 gtaaaaagtg ctgaaa 376

<210> 189
 <211> 501
 <212> DNA
 <213> Homo sapien

<400> 189
 cccctaccgc ggagcagcac catgtcggcg ccggcgcca aagtcagtaa aaaggagctc 60

60

```

aactccaacc acgacggggc cgacgagacc tcagaaaaag aacagcaaga agcgattgaa 120
cacattgatg aagtacaaaa tgaaatagac agacttaatg aacaagccag tgaggagatt 180
ttgaaagtag aacagaaata taacaaactc cgccaacat tttttcagaa gaggtcagaa 240
ttgatcgcca aaatcccaaa tttttgggta acaacatttg tcaaccatcc acaagtgtct 300
gcactgcttg gggaggaaga tgaagaggca ctgcattatt tgaccagagt tgaagtgaca 360
gaatttgaag atattaaatc aggttacaga atagattttt attttgatga aaatccttac 420
tttgaataa aagttctctc caaagaattt catctgaatg agagtgggtga tccatcttcg 480
aagtcaccg aaatcaaata g 501

```

<210> 190

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 190

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aagttctgaa gattcatttt tgtctgccat tataaattat actaatagct ctacagtcca 60
ctttaagttg tcccctacat atgtattata tatggcatgc cggtatgtat tgtccaacca 120
gtacagacct gacatcagcc ctacagagcg cacacataaa gtcattgcag tcgtcaacaa 180
gatggtgagc atgatggagg gtgtcatcca gaaacagaag aatattgcag gggcacttgc 240
cttctggatg gcaaattgcat ctgaacttct caacttcatt aagcaagacc gagaccttag 300
tcggatcaca ctggatgctc aagatgtttt agcacatttg gttcaaattg catttaata 360
cttggttcac tgtcttcaat cagaacttaa taattacatg ccagccttcc tagatgaccc 420
tgaagagaac agtctgcaac gaccaaaaaat agatgatgtg ctgcacacgc tcacaggagc 480
catgtntctg ctacgacgct g 501

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<210> 191

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 191

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ttgtgcgtgc tcagccacta ccctttcttn gnccactttc cganagtgtt tgtatactct 60
caagcgcctg gnggactgct gtagtgagcg ctttctgggc aagaaactgg gcatccctcg 120
aggcgtaaaa agggacacca tgtggcggat ctttactgga tcgctgctgg tagaggagaa 180
gtcaagtgcc cttctgcatg accttcgaga gattgaggcc tggatctatc gattgctgcg 240
ctccccagta cccgtctctg ggcagaagcg agtagacatc gaggtcctac cccaagagct 300
ccagccagct ctgacctttg ctcttccaga cccatctcga ttcaccctag tggatttccc 360
actgcacctt cccttgaac ttgtagggtg ggacgcctgt ctccagntgc taacctgcat 420
tctggtagag cacaaggcgg cgctacagtc ccgagactac aatgcactct ccatgtctgt 480
gatggcatnc atggcaatga t 501

```

<210> 192

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

61

<223> n = A,T,C or G

<400> 192

tttgantttga	accagaagct	ccaggaagaa	aaacataaaa	gcataactga	ggcacttagg	60
agacaggagc	agaatataaa	gagttttgag	gagacctatg	accgaaagct	caagaatgaa	120
cttctaaact	tccacaggct	gcatggtgtc	tgcttggtct	tggaatcct	catatgactt	180
tggcaggtgt	tgaggttttg	aggctcttcg	ccacaggagt	gcttctattt	ccttttggaa	240
ccaaaagggc	agctggtaac	agctgggaaa	gggaagtga	actgtgaaaa	tgtgcctttt	300
ggtattgcta	atccggatat	aatgctcttg	gcagttggct	ctcaggactg	tgcttagtcc	360
ctgagcacia	aagttcttac	cttggttggg	ggtgggcaga	tggtacaggt	ggattggaag	420
tgaccgtctg	attatcattt	gggattgagt	ctgttgtgtg	ctgtgtaaat	ttaatttacc	480
cctttgtctt	ttgtgtcagt	t				501

<210> 193

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 193

agntttctgc	tctgcctgc	ctgcccgtc	ccttgcttgc	tgcgccttgc	gctcgccctc	60
tctcgagga	tgcaggggac	tctgaccaca	gcctgtggct	gggaaggag	acagaggcgg	120
cgcggtctca	ggggaacga	ggctgcagt	gtggtagtag	gaagatgtcg	ggcgaggacg	180
agcaacagga	gcaactatc	gctgaggacc	tggtcgtgac	caagtataag	atggggggcg	240
acatcgccaa	caggggtact	cggtccttgg	tggaagcatc	tagctcaggt	gtgtcggtac	300
tgagcctgtg	tgagaaaggt	gatgccatga	ttatggaaag	aacagggaaa	atcttcaaga	360
aagaaaagga	aatgaagaaa	ggtattgctt	ttcccaccag	catttcggta	aataactgtg	420
tatgtcactt	ctcccctttg	aagagcgacc	aggattatat	tctcaaggaa	ggtgacttgg	480
taaaaattga	ccttgggggc	c				501

<210> 194

<211> 560

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(560)

<223> n = A,T,C or G

<400> 194

ggcttcactc	tcacaaactc	cttgaatttc	ttctctttat	tcttttctct	gtcttttgta	60
gttggggaac	tgcanagac	ccgcttcctg	gtcagggctc	cctggctggg	cttgtctgaa	120
gctgaagggc	ccctggtttg	gacatgcctc	tttccggggc	tctcttctgg	ctccagtgc	180
ttctccattc	catggaaata	cttcatgtga	tagtgcaaca	gtttggcttt	gcggaaaaat	240
tttaaacagt	ccacaacttt	gcatctaaac	ttatggtcta	ggtcgacagc	tggtgcatta	300
natgacccaa	aatcatctgt	tttcttaaaa	gtatttggtt	cttccacagt	cgaaatctct	360
tgtaattcca	caaggggaga	agtcggttct	gttttcacgc	tgttttctcc	cattgatggg	420
cagttcaact	ccaagcctgc	agccccgat	ccatcccaaa	aggagnggca	agtcagtgc	480
natganacct	ggccagcttc	caaagcagac	ttcaactgac	cttcttcaga	ttccttggtg	540
ctanacaacg	tgtcttgcaa					560

<210> 195

<211> 582

<212> DNA

62

<213> Homo sapien

<400> 195

ggcacctggg	gagaaatgga	tgagagaagg	acctggctgg	aaagcctttg	ccccgctgct	60
ctgctccgcc	cataagagga	cccctgaaat	gtcccgtgca	gtttgttcaa	gtcccctgtg	120
tgatgaaatg	tgccctctgc	cttaccctgt	tgagaatacc	tgtgggtgtg	cagcgagtat	180
tttggatatt	gacctgtcca	aagacgactt	gatacctcta	taatgtaaca	gaaaagggtca	240
gaaaatatta	agcaagtaga	agtgtggagc	atattaagca	agatgaacat	ctcggaagc	300
agctgtggaa	gccctaactc	tgagatac	tctagtact	ttaaggacct	ttggacaaaa	360
ctaaaagaat	gtcatgatag	agaagtacaa	ggtttacaag	taaaagtaac	caagctaaaa	420
caggaacgaa	tcttagatgc	acaaagacta	gaagaattct	tcaccaaaaa	tcaacagctg	480
agggaaacagc	agaaagtctt	tcatgaaacc	attaaagttt	tagaagatcg	gttaagagca	540
ggcttatgtg	atcgctgtgc	agtaactgaa	gaacatatgc	gg		582

<210> 196

<211> 401

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 196

aaaccaaaga	atggattgaa	gagaagaatc	aagctctaaa	cacagacaat	tatggacatg	60
atctcgccag	tgtccaggcc	ctgcaacgca	agcatgagg	cttcgagagg	gaccttgccg	120
ctctcggtga	caaggtaaac	tcccttggtg	aaacagcaga	gcgcctgata	cagtcccatc	180
ccgagtcagc	agaagacctg	caggaaaagt	gcacagagtt	aaaccaggcc	tgagcagacc	240
tggggaaacg	tgagatcag	cgcaaggcaa	agttgggtga	ctcccacgac	ctgcagcgct	300
tccttagcga	tttccggggc	ctcatgtctt	ggatcaatgg	aatacggggg	ttggtgtcct	360
cagatgagct	anccaaggat	gtcaccggag	ctgangcatt	g		401

<210> 197

<211> 457

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(457)

<223> n = A,T,C or G

<400> 197

agttttcccg	accatggcca	acctggagcg	caccttcata	gccatcaagc	cggacggngt	60
gcancgcggc	ctggtggg	agatcatcaa	gcgcttngan	cagaagggat	tcgcctctnt	120
ggccatgaan	ttcttcggg	cctctgaana	acacctgaag	cagcactaca	ttgacctgaa	180
agaccgacca	ttcttcctg	ggctggtgaa	ntacatgaac	tcaggggccg	ttgtggccat	240
ggtctgggag	gggctgaacg	tggtgaagac	aggccgagtg	atgcttgggg	agaccaatcc	300
agnagattca	aagccaggca	ccattcnttg	ggacttctgc	attcagggtg	gnangaacat	360
nattcatggn	agtgattcan	taaaaagtgc	tgaaaaaana	atcancctat	ggnttaagcc	420
tgaagaactg	gttgactaca	agtccttngc	tcatgac			457

<210> 198

<211> 474

<212> DNA

<213> Homo sapien

<400> 198

63

aggctgaacc	cgaggagatg	aacccttta	ctaagggtgaa	gctgatcaac	gagctgaatg	60
aacgagaggt	ccagcttggg	gtggccgata	aggtgtcctg	gcactccgag	tacaaggaca	120
gcgcctggat	cttcctggga	gggcttcctt	atgaactgac	tgaaggggac	atcatctgtg	180
tgttctcaca	atatggggag	attgttaaca	ttaatctcgt	gcgggacaag	aaaactggga	240
aatccaaagg	attctgtttc	ctctgctatg	aagaccagag	gagcacaatt	ctggccgtcg	300
acaattttta	tgggatcaag	atcaaaggaa	gaactatccg	agtggatcat	gtgtctaact	360
atcgggctcc	taaggactca	gaagaaatag	atgatgtgac	cagacaactc	caggagaagg	420
gctgtggggc	tcgtaccccc	tcaccaagtt	tgtctgagag	ctctgaagat	gaaa	474

<210> 199

<211> 574

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(574)

<223> n = A,T,C or G

<400> 199

gagaagaaac	aggaagaaga	agaaacgatg	cagcaagcga	catgggtaaa	atacacattt	60
ccagttaagc	atcaggtttg	gaaacaaaaa	ggtgaagagt	acagagtgcg	aggatatggt	120
ggttggagct	ggattagtaa	aactcatgtt	tataggtttg	ttcctaaatt	gccaggcaat	180
actaatgtga	attacagaaa	gtcgttagaa	ggaaatgtga	aggagctctt	agattctgac	240
agtataaaac	cctgcaagga	agaaccaatg	gaagtagacg	atgacatgaa	aacagagtca	300
catgtaaatt	gtcaggagag	ttctcaagta	gatgtgggtc	atgttagtga	gggttttcat	360
ctaaggacta	gttacaaaaa	gaaaacaaaa	tcattccaaac	tagatggact	tcttgaaagg	420
agaattaaac	agttttacact	ggaagaaaaa	cagcgactcg	aaaaaatcaa	gttggagggt	480
ggaattaaag	gtataaggaa	agacttctac	aaattcttca	aaaaatctct	ctgaatcacc	540
agtaataaac	gaaagcaaaa	gaanggtgtc	agag			574

<210> 200

<211> 522

<212> DNA

<213> Homo sapien

<400> 200

tcataaacct	tatggagaga	aaggactttg	agacatggct	tgataacatt	tctgtttacat	60
ttctttctct	gacggacttg	cagaaaaaatg	aaactctgga	tcacctgatt	agtctgagt	120
gggcagtcca	gctcaggcat	ctctccaata	acctagagac	tctcctcaag	cgggacttcc	180
tcaaaactct	tcccctggag	ctcagttttt	atttgttaaa	atggctcgat	cctcagactt	240
tactcacatg	ctgcctcgtc	tctaaacagt	ggaataagggt	gataagtgcc	tgtacagagg	300
tgtggcgagc	tgcatgtaaa	aatttgggct	ggcagataga	tgattctgtt	caggacgctt	360
tgacttgga	gaaggtttat	ttgaaggcta	ttttgagaat	gaagcaactg	gaggaccatg	420
aagcctttga	aacctcgta	ttaattggac	acagtgccag	agtgtatgca	ctttactaca	480
aagatggact	tctctgtaca	gggtcagatg	acttgcgtgca	aa		522

<210> 201

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 201

atctccgcct	gggttcggccc	gcctgcctcc	actcctgcct	ctaccatgtc	catcagggtg	60
------------	-------------	------------	------------	------------	------------	----

64

accagaagt	cctacaaggt	gtccacctct	ggcccccg	ccttcagcag	ccgtcctac	120
acgagtggg	ccggttccc	catcagctcc	togagcttct	cccagtgagg	cagcagcaac	180
tttcgcggtg	gcctgggcgg	cggctatggt	ggggccagcg	gcatgggagg	catcaccgca	240
gttacggtca	accagagcct	gctgagcccc	cttgtccttg	aggtggaccc	caacatccag	300
gccgtgcga	cccaggagaa	ggagcagatc	aagacctca	acaacaagtt	tgctccttc	360
atagacaagg	tacggttcct	ggagcancag	aacaagatgc	tggagaccaa	gtggagcctt	420
cttgacgag	cagaagacgg	ctcgaagcaa	catggacaac	atgttcnaaa	gtacatcaa	480
caaccttagg	cgnagcttga	a				501

<210> 202

<211> 501

<212> DNA

<213> Homo sapien

<400> 202

gcgttctgtg	gagagagtgc	gaggtcaggc	catgaacttg	ggagatgggt	taaagcttga	60
aactaaatta	ctggatggaa	aaaccaagct	aatattgtct	ccatatgaac	ataaatcaaa	120
aatttctgtg	aagatgggaa	ataaggccaa	gattgcaaaa	tgtcctttta	gaacaaaaac	180
tgggcacatt	ctaaaaatcaa	cacaagatac	ttgtattggg	agtgaacaa	ttttgcaaaa	240
gaagccagtt	ggttcagaaa	catcacaggc	aaaaggtgaa	aaaaatggaa	tgactttttc	300
atccactaag	gatttatgta	aacaatgtat	agataaagac	tgtcttcata	tccagaaaga	360
gatttcacct	gcaactccta	atatgcagaa	gactagaaac	accgtaaata	catctctagt	420
aggtaaacag	aagcctcaca	aaaaacacat	cacagctgaa	aacatgaaga	gcagtttggt	480
gtgtctaaca	caagaccaac	t				501

<210> 203

<211> 395

<212> DNA

<213> Homo sapien

<400> 203

cttcatcatt	gcagactcct	tcctacatca	tgcgtatcgt	tttcattata	cactttgtgc	60
cactttgctg	ctagccttca	agggattgca	cagctacttc	attacagtaa	cagaagagat	120
tccttcttgt	cagaaactag	aactggccaa	ggccaacatg	cagctcctat	atgagcgtct	180
tctcagaaga	aaacagctac	gaacacagaa	agacaaccat	ctagaggaaa	tggatgtaga	240
agctcgactt	actgaactat	gtgaagaagt	taagaaaaata	gagaatcctg	atgaactggc	300
agaacttata	aatatgaatc	ttgcgcaact	ttgctcactt	ttgatggctt	tatggggaca	360
gtttctggaa	gttataacgc	tacacgaaga	actaa			395

<210> 204

<211> 501

<212> DNA

<213> Homo sapien

<400> 204

aggtcaggca	gaaattggag	agggggctca	aaagctgctg	cggcccaaca	gcttgagact	60
ggcaagtgc	tcagatgcag	agtcagactc	tcgggcaagc	tctcccaact	ccaccgtctc	120
caacaccagc	accgagggct	tcgggggcat	catgtctttt	gccagcagcc	tctatcggaa	180
ccacagtacc	agcttcagtc	tttcaaacct	cacactgccc	accaaagggtg	cccagagaaa	240
ggccacgccc	ttcccagtc	tgaaaggaaa	caggagggcg	ttagtggatc	agaagtcatc	300
tgtcattaaa	cacagcccaa	cagtgaataa	agaacctcca	tcaccccagg	gtcgatccag	360
caattctagt	gagaaccagc	agttcctgaa	ggaggtgggtg	cacagcgtgc	tggacggcca	420
gggagttggc	tggctcaaca	tgaaaaaggt	gcgccggctg	ctggagagcg	agcagctgcg	480
agtctttgtc	ctgagcaagc	t				501

<210> 205

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 205

cagaagtgca	gcggtggcgg	cggctggttg	cgggcccggc	gcgggctggc	ggagatggag	60
gatcttgttc	aagatggggg	ggcttcacca	gctacccctg	ggaccgggaa	atctaagaat	120
tgagagaaaga	aattgaagaa	ctcagatcaa	aacctgttac	tgaagggaact	ggtgatatta	180
ttaaggcatt	aactgaacgt	ctggatgctc	ttcttctgga	aaaagcagag	actgagcaac	240
agtgtctttc	tctgaaaaag	gaaaatataa	aaatgaagca	agaggttgag	gattctgtaa	300
caaagatggg	agatgcacat	aaggagttgg	aacaatcaca	tataaactat	gtgaaagaaa	360
ttgaaaattt	gaaaaatgag	ttgatggcag	tacgttccaa	atacagtga	gacaaagcta	420
acttacaaaa	ncagctggaa	naagcaatga	atacncaatt	agaactttca	naacaactta	480
aatttcanaa	caactctgaa	g				501

<210> 206

<211> 599

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(599)

<223> n = A,T,C or G

<400> 206

tggtcgcacc	agctctctgc	tctcccagcg	cagcgccggc	gcccggcccc	tccagcttcc	60
cggaccatgg	ccaacctgga	gcgcaccttc	atcgccatca	agccggacgg	cgtgcagcgc	120
ggcctggtgg	gcgagatcat	caagcgcttc	gagcagaagg	gattccgcct	cgtggccatg	180
aagttcctcc	gggcctctga	agaacacctg	aagcagcact	acattgaact	gaaagaccga	240
ccattcttcc	ctgggctggt	gaagtacatg	aactcagggc	cggttgtggc	catggtctgg	300
gaggggctga	acgtggtgaa	gacaggccga	gtgatgcttg	gggagaccaa	tccagcagat	360
tcaaagccag	gcaccattcg	tggggacttc	tgcattcagg	ttggcaggaa	catcattcat	420
ggcagtgatt	cagtaaaaaag	tgctgaaaaa	gaaatcagcc	tatggtttaa	gcctgaagaa	480
ctggttgact	acaagtcttg	tgctcatgac	tgggtctatg	aataagaggt	ggacacaaca	540
gcagttctct	tcacacggcg	tggtgtgtcc	tggaacacagt	nttattcttg	acttaaagc	599

<210> 207

<211> 395

<212> DNA

<213> Homo sapien

<400> 207

ccggccgggg	cgagggtcgg	cggccgcccg	cgggcccggc	ccgcgcacag	cgcccgcattg	60
tacaacatga	tggagacgga	gctgaagccg	ccgggcccgc	agcaaacttc	ggggggcggc	120
ggcggcaact	ccaccgcggc	ggcggccggc	ggcaaccaga	aaaacagccc	ggaccgcgtc	180
aagcggccca	tgaatgcctt	catggtgtgg	tcccgcgggc	agcggcgcaa	gatggcccag	240
gagaacccca	agatgcacaa	ctcggagatc	agcaagcgcc	tgggcgcoga	gtggaaactt	300
ttgtcggaga	cggagaagcg	gccgttcacg	gacgaggcta	agcggctgcg	agcgtgcac	360
atgaaggagc	accgggatta	taaataccgg	ccccg			395

<210> 208

<211> 398

<212> DNA

<213> Homo sapien

<400> 208

66

aggctctcca	agccctgctg	ttatatTTTT	ccaggaggga	ggggcgattc	tgccttgttt	60
gcagtgaatg	gtttcaatat	gctcatcaat	ggcggatcag	agagaaaatc	ctgcttctgg	120
aagctcatcc	gacacttaga	ccgagtggac	tccatcctgc	tcacccacat	tggggatgac	180
aatttgccctg	gaataaacag	catgttacag	cggaaaattg	cagagctcga	ggaagaacag	240
tcccagggct	ccaccacaaa	tagtgactgg	atgaaaaacc	tcattctccc	tgacttagga	300
gttgatattc	tcaatgtacc	tgaaaatctc	aaaaatccag	agccaaacat	caagatgaag	360
agaagcatag	aagaagcctg	cttcactctc	cagtaacct			398

<210> 209

<211> 501

<212> DNA

<213> Homo sapien

<400> 209

gcgcagcctc	ctgggagttg	tagtcgcgat	cctgaggtaa	cggataagtt	tataccatgg	60
atagcacaaa	ggagaagtgt	gacagttaca	aagatgatct	tctgcttagg	atgggactta	120
atgataataa	agcaggaatg	gaaggattag	ataaagagaa	aattaacaaa	attataatgg	180
aagccacgaa	gggtccaga	ttttatggaa	atgagctcaa	gaaagaaaag	caagtcaacc	240
aacgaattga	aaatatgatg	caacaaaaag	ctcaaatac	cagccaacag	ctaagaaaag	300
cacaattaca	ggttgacaga	tttgcaatgg	aattagaaca	aagccgaaat	ttgagcaata	360
ccatagtgca	cattgacatg	gatgctttct	atgcagctgt	agaaatgagg	gacaatccag	420
aattgaagga	taaaccatt	gctgtaggat	caatgagtat	gctgtctact	tcaaattacc	480
atgcaaggag	atttggtggt	c				501

<210> 210

<211> 450

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)... (450)

<223> n = A,T,C or G

<400> 210

cggacaagt	gcagaacagg	ataatcggtt	cagcaacaaa	cagaagaaac	tactgaagca	60
gctgaaat	gcagaatgcc	tagaaaaaaa	ggtggacatg	agcaaagtaa	atttgagggt	120
tataaagcct	tgataacaa	aaagagtaac	ggaaatcctt	gggtttgaag	atgatgttgt	180
gattgagttt	atattcaacc	agctggaagt	gaagaatcca	gactccaaaa	tgatgcaaat	240
caacctgact	ggatttttga	atggaaaaaa	tgctcgagaa	tttatgggag	aactgtggcc	300
cctgctgcta	agtgcacaag	aaaacatcgc	gggaatccct	tctgctttcc	tagaactgaa	360
gaaagaagaa	ataaaacaaa	gacagattga	acaagaaaaa	ctggcatcta	tgaaaaagcn	420
agatgaagac	caagattaaa	gagaaangga				450

<210> 211

<211> 601

<212> DNA

<213> Homo sapien

<400> 211

ctcagagcag	ctggaacagg	ccaagcggtt	caaagcaaat	ctagagaaga	acaagcaggg	60
cctggagaca	gataacaagg	agctggcgtg	tgagggtgaag	gtcctgcagc	aggtcaaggc	120
tgagtctgag	cacaagagga	agaagctcga	cgcgaggtc	caggagctcc	atgccaaagg	180
ctctgaaggc	gacaggctca	gggtggagct	ggcggagaaa	gcaagtaagc	tgcagaatga	240
gctagataat	gtctccaccc	ttctggaaga	agcagagaag	aagggtatta	aatttgctaa	300
ggatgcagct	agtcttgagt	ctcaactaca	ggatacacag	gagcttcttc	aggaggagac	360
acgcagagaa	ctaaacctga	gcagtcggat	cgggcagctg	gaagaggaga	agaacagtct	420
tcaggagcag	caggaggagg	aggaggaggt	caggagaagc	ctggagaagc	aagtgcctgg	480
cctgcagctc	cagttggctg	ataccaagaa	gaaagtagat	gacgacctgg	gaacaattga	540

67

aagtcttgga agaagccaag aagaacttct gaaggacgcg gagggcctga gccaacgcct 600
g 601

<210> 212

<211> 498

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(498)

<223> n = A,T,C or G

<400> 212

atgacaaata	ttccacatct	gtgattctct	ccagtcaaaa	gttctttgag	acgatgccat	60
cggccttggc	caatcggaga	atggaatcat	ctgactcacc	catcctacga	atggccccgc	120
agatagcata	agttttaaac	tggccattaa	acctgcctgt	gaccttgta	acctcggcca	180
cgttcatctg	gatggatgcg	tggtccttgg	caccgatgat	gcgattgcta	gcggagcatt	240
tccggcgcac	gtacagggtcc	acgaactcgc	cggcgctcgtt	ctgcatttcg	aggctgggct	300
gcgcctgctg	ccactcgtgc	cgaattcttt	ggtccacta	gtgtcgacct	gcaggcgcgc	360
gagctccagc	ttttgtccct	ttagtgaggg	ttaatttcga	gcttggcgta	atcaanggca	420
tagctggttc	ctgngngaaa	ttggtatccg	tcacaattcc	ncncaatata	cgagccggaa	480
gtataaaggg	naaagcct					498

<210> 213

<211> 601

<212> DNA

<213> Homo sapien

<400> 213

actaccagac	aaccttagcc	aaaccattta	cccaaataaa	gtataggcga	tagaaattga	60
aacctggcgc	aatagatata	gtaccgcaag	ggaaagatga	aaaattataa	ccaagcataa	120
tatagcaagg	actaaccctt	ataccttctg	cataatgaat	taactagaaa	taactttgca	180
aggagagcca	aagctaagac	ccccgaaacc	agacgagcta	cctaagaaca	gctaaaagag	240
cacacccgtc	tatgtagcaa	aatagtggga	agattttatag	gtataggcga	caaacctacc	300
gagcctgggtg	atagctgggt	gtccaagata	gaatcttagt	tcaactttta	atttgccac	360
agaaccctct	aatcccctt	gtaaatttaa	ctgttagtcc	aaagaggaac	agctctttgg	420
acactaggaa	aaaaccttgt	agagagagta	aaaaatttaa	cacctatagt	aggcctaaaa	480
gcagccacca	attaagaaag	cgttcaagct	caacacccac	tacctaaaaa	atcccaaaca	540
tatactgaac	tcctcaacct	aattggccaa	tctatcccct	atagaagact	aatggtagta	600
t						601

<210> 214

<211> 500

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(500)

<223> n = A,T,C or G

<400> 214

aggctgcatt	tacgggggtct	cccgaggggc	cagagtcgtg	gcttacagaa	gagacgaaat	60
gtggctctgag	ggacgatatg	aatatgaaag	aattccgaga	gaacgagcac	ctcctcgaag	120
tcatcccagt	gatgaatctg	gttatagatg	gacaagagac	gatcattctg	caagcaggca	180
acctgaatac	agggacatga	gagatggctt	tagaagaaaa	agtttctact	cttcccatta	240
tgogagagag	cggtctcctt	ataaaaaggga	caatactttt	ttcagagaat	cacctgttgg	300
-cogaaaggat	tctccacaca	gcanatctgg	ttccagtgtc	agtagcanaa	gctctctcca	360

68

gaaaggagca	aatcatactc	tttccatcag	tctcaacata	gaaataaaga	gaggcctgtc	420
agtctttgaa	aacatcaaga	gatacttccc	ctcaagtggg	tcacagttct	tctcaaaggg	480
gtagacaaac	ccagtaggta					500

<210> 215

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 215

gcctgtggga	gcccgtggcc	tttaaagtgc	cgttcagcct	tttcctccag	gggtgctttg	60
taaacacggc	tgtgctcagg	gctcgcgggt	gaccgaaagg	atcatgaact	agtgacctgg	120
aaaggggtact	agatggaaac	ttgagaaagg	actgcttatt	gataacagct	aagggtattcc	180
tggaagcaga	gtaaataaaag	ctcatggccc	accagctaga	aagtattctt	gccatgagaa	240
aaagaatgtg	ataagttatt	caacttatga	aattcaagtt	acatgtgaat	tctgccaggc	300
aatacaagga	cctgtggaat	atgagtgatg	acaaaccctt	tctatgtact	gcgcctggat	360
gtggccagcg	ttttaccaac	gaggatcatt	tggtgtgtcca	taaacataaa	catgagatga	420
cactgaaatt	tggtccanca	cgtaatgaca	gtgtcattgt	ggctgatcag	accccaacac	480
caacaagatt	cttgaaaaac	t				501

<210> 216

<211> 501

<212> DNA

<213> Homo sapien

<400> 216

aggcggcctt	gggggcatct	gcattggagt	tggggggtgcc	gatgctgtgg	atgtcatggc	60
tgggatcccc	tgggagttga	agtgccccaa	ggtgattggc	gtgaagctga	cgggctctct	120
ctccggttgg	tcctcaccca	aagatgtgat	cctgaagggtg	gcaggcatcc	tcacgggtgaa	180
aggtggcaca	ggtgcaatcg	tggaatacca	cgggcctggg	gtagactcca	tctcctgcac	240
tggtcatggcg	acaatctgca	acatgggtgc	agaaattggg	gccaccactt	ccgtgttccc	300
ttacaaccac	aggatgaaga	agtacctgag	caagaccggc	cgggaagaca	ttgccaatct	360
agctgatgaa	ttcaaggatc	acttggtgcc	tgaccctggc	tgccattatg	accaactaat	420
tgaaatatac	ctcagtgagc	tgaagccaca	catcaatggg	cccttcaccc	ctgacctgct	480
caccctgtgg	cagaagtggg	c				501

<210> 217

<211> 408

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(408)

<223> n = A,T,C or G

<400> 217

gctacacctg	gacgtgacgt	ggggctggga	gcactggggc	gggatcctgc	cacagtcgct	60
ggacctgttg	ctctgcatca	acatggccca	tgctcagccc	ctgcgctgca	cggaggaacc	120
cagaatgggg	gcttcggggac	acagccctcc	tgaggagacct	gggaaaggcc	agtggcctgc	180
tcttgagag	gatggtggac	atgccagcca	acaacaaatg	cctgatcttc	cggaaaaact	240
aagccctcc	ttcaccccg	cacacctgca	tcctgcggg	angctctgtg	aggcacgaac	300
cctgcctccc	taggccggac	cttgtggacg	acagcccccac	ccagtctgtg	ctctcagccg	360
ntggccgaag	ggccancct	gctcagaata	aacatgtcct	gctgcccgg		408

<210> 218
 <211> 402
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(402)
 <223> n = A,T,C or G

```
<400> 218
tgcttgtctc aaagattaaag ccatgcatgt ctaagtacgc acggccggta tctgtctccg      60
cctgccgcag gnggccatgg ntaccgggca ggngttgttc cagcggttct tttataccaa      120
gtccttcgtg aagcactcca tggagcatgt gtcaatggcc tgtgtccacc tggccttcaa      180
gatagaagag gccccaagac gcatacggga cgtcatcaat gtgtttcacc cgccttcgac      240
agctgagaga caaaaagaag cccgtgcctc tactactgga tcaagattat gttaatttaa      300
agaacccaat tataaaggcg ggnaagacna ttcttcaaaa agatgggntt ctgcgncat      360
gtgaagcatn ctcataagan aatcgntatg taccttcagg gg                               402
```

<210> 219
 <211> 486
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(486)
 <223> n = A,T,C or G

```
<400> 219
aatgctgcgg agattgaggt gtcggttcgt gctgctgagc tgcccaggct tcacggagcg      60
gtgttggaag tcaatagctc ttctagcctt tgcattgttt aaatataata gtgtcattgg      120
actaagatgt tctgatgcc aacctcttca gagttaaaca gtgggcagaa cttcctaacc      180
cagtggatga ccaatccttc tcgggctggg gtcataattaa atcgtggatt tctatatttg      240
gaagcagaca aagagaagcg agcagcttgt ggacatttct accagctttt nctattaaaa      300
ggcacacatt tttctgatag cttcagcttt tataaatgaa gaaaaattca cttcttgaag      360
aacagaagtt ggagtcaaac aacacttaca aaccacagtc agataaatct gaaaccata      420
cagcctttcc ttgcattaaa aagggaccnc aggtngcggn atggtccagt gctcctggac      480
ncccgg                               486
```

<210> 220
 <211> 380
 <212> DNA
 <213> Homo sapien

```
<400> 220
ggcggattag ccttcgcggg gcaaaatgga gctcgaggcc atgagcagat ataccagccc      60
agtgaaccca gctgtcttcc cccatctgac cgtggtgctt ttggccattg gcatgttctt      120
cacgccttgg ttcttcgttt acgaggtcac ctctaccaag tacactcgtg atatctataa      180
agagctcctc atctccttag tggcctcact cttcatgggc tttggagtcc tcttcctgct      240
gctctggggt ggcatctacg tgtgagcacc caagggtaac aaccagatgg cttcactgaa      300
acctgctttt gtaaattact tttttttact gttgctggaa gtgtcccacc tgctgctcat      360
aataaatgca gatgtatagc                               380
```

<210> 221
 <211> 406
 <212> DNA
 <213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(406)

<223> n = A,T,C or G

<400> 221

gcggattagc	cttcgcgggg	caaaatggag	ctcgaggcca	tgagcagata	taccagccca	60
gtgaaccag	ctgtcttccc	ccatctgacc	gtgggtgcttt	tggccattgg	catgttcttc	120
accgcctggt	tcttcgttta	cgangtcacc	tctaccaagt	acactcgtga	tatctataaa	180
gagctcctca	tctccttagt	ggcctcactc	ttcatgggct	ttggagtcct	cttcctgctg	240
ctctgggttg	gcactctacgt	gtgagcacc	aagggttaaca	accagatggc	ttcactgaaa	300
cctgcttttg	taaattactt	ttttttactg	ttgctggaag	tgtcccacct	gctgctcata	360
ataaatgcag	atgtatagcc	ctatagnag	cgtattacaa	ttcact		406

<210> 222

<211> 501

<212> DNA

<213> Homo sapien

<400> 222

aatggcggta	gttgggtgtgt	cctcgggttc	tcgggtgctg	ggtcgggtccc	gcccacagct	60
ggggcggcct	atgtcgagtg	gcgcccattg	cgaagagggc	tcagctcgca	tgtggaagac	120
tctcaccttc	ttcgtcgcg	tccccggggt	ggcagtcagc	atgctgaatg	tgtacctgaa	180
gtcgcaccac	ggagagcacg	agagaccgga	gttcacgcgc	tacccccatc	tccgcatcag	240
gaccaagccg	tttcctggg	gagatggtaa	ccatactcta	ttccataacc	ctcatgtgaa	300
tccacttcca	actggctacg	aagatgaata	aagagaatct	ggaccactac	ccgggcacca	360
gggaccacag	cactgggtttg	gaccgttact	ctgcacatgg	accagaaaaa	gtatatggga	420
ccttaagctc	accttcttta	cttgtatcaa	atgatgactg	gtatactggg	ctcccatccc	480
tttgcttggtg	gcaggagatg	g				501

<210> 223

<211> 455

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(455)

<223> n = A,T,C or G

<400> 223

aatcttatgc	aaaagggaca	caggggttca	aaaataaaaa	tttctcttcc	ccctcccaa	60
acctgtaccc	cagctccccg	accacaacc	ccttcctccc	ccgggggaaag	caagaaggag	120
caggtgtggc	atctgcagct	gggaananag	aggccgggga	ggtgccgagc	tcgggtgctgg	180
tctctttcca	aatataaata	cgtgtgtcan	aactggaaaa	tcctccagca	cccaccacc	240
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cggctggctg	cgggtctactg	catccgctgg	gtgtgcaccc	cgcgagcctc	ctgctgctca	360
ttgtagaaga	gatgacactc	ggggtccccc	ccggtggng	ggggctccct	ggatcagctt	420
tccgngngnt	gggggttcaca	caccagcact	tccca			455

<210> 224

<211> 507

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(507)

71

<223> n = A,T,C or G

<400> 224

ttaccacac	ccattgtagc	ccttgggtgn	gggatgtgcc	ctgtccctgc	agggccaaaa	60
gggtccatgt	ttccctcaaa	tctcaaagca	gtcctggccc	aggctgcagg	caggagggaa	120
gtcgtgacct	cctggcaggc	tcagtcctgc	agctgcccc	agcagccana	ctgtccctgg	180
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tgcatgatct	cttcacacct	ggggctctgc	aggaggagct	ggntctctcc	caccctcaag	360
gccagggtgn	gggggcccac	tagctggcag	gcggccacat	ggccatagct	gacactgnng	420
atgggctccg	tctcccctgg	ccggganagg	gacatggcct	tggtcccaa	gcccaggcac	480
agtttntggg	ggagcacccc	gaccagg				507

<210> 225

<211> 572

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(572)

<223> n = A,T,C or G

<400> 225

aaacctccct	taaagattct	ttgatgcttt	gctctatcac	tgtnacctg	gtctttttcc	60
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ccatcacagt	acaaaaatac	ccccaaaat	gaagttcaaa	tttgatcaaa	acataaatca	180
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tggtaacacg	tgccagccac	cggggccctg	agtcataact	ttttacggaa	ggacgccacc	480
ttgaattttg	cacgnggnc	tccanancgg	ttgctgaaga	tgggctcntc	acactttagc	540
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<210> 226

<211> 401

<212> DNA

<213> Homo sapien

<400> 226

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tcgtacgcct	tcttcgtgca	gacctgccgg	gaagagcaca	agaagaaaca	cccggactct	180
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aaggagaagt	cgaagtttga	agatatggca	aaaagtgcac	aagctcgcta	tgacaggggag	300
atgaaaaatt	acgttcctcc	caaaggatgat	aagaagggga	agaaaaagga	ccccaatgct	360
cctaaaaggc	caccatctgc	cttcttctgt	tttgcctctga	a		401

<210> 227

<211> 501

<212> DNA

<213> Homo sapien

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

72

<400> 227
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 tgcagagcaa ttggtggtgg agctaaaaga tattattaga cagaaggatg ttcaactgca 240
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 aagataacat antcagagag gagactatca ncttgagcca ntctcagcca gagacacctg 480
 acagaatggg tgtgaaggag c 501

<210> 228
 <211> 501
 <212> DNA
 <213> Homo sapien

<220>
 <221> misc_feature
 <222> (1)...(501)
 <223> n = A,T,C or G

<400> 228
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 ttcagaaaaca gctagaacag attcgtaaac aacagaaaga acatgctgaa ttgattgaag 420
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 tccagcccca nccccctaa t 501

<210> 229
 <211> 4099
 <212> DNA
 <213> Homo sapiens

<400> 229
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<210> 230

<211> 2649

<212> DNA

<213> Homo sapiens

<400> 230

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 <213> Homo sapiens

<400> 234
 Met Tyr Ile Lys Met Ala Thr Leu Ala Asn Gly Gln Ala Asp Asn Ala
 5 10 15
 Ser Leu Ser Thr Asn Gly Leu Gly Ser Ser Pro Gly Ser Ala Gly His
 20 25 30
 Met Asn Gly Leu Ser His Ser Pro Gly Asn Pro Ser Thr Ile Pro Met
 35 40 45
 Lys Asp His Asp Ala Ile Lys Leu Phe Ile Gly Gln Ile Pro Arg Asn
 50 55 60
 Leu Asp Glu Lys Asp Leu Lys Pro Leu Phe Glu Glu Phe Gly Lys Ile
 65 70 75 80
 Tyr Glu Leu Thr Val Leu Lys Asp Arg Phe Thr Gly Met His Lys Gly
 85 90 95
 Cys Ala Phe Leu Thr Tyr Cys Glu Arg Glu Ser Ala Leu Lys Ala Gln
 100 105 110
 Ser Ala Leu His Glu Gln Lys Thr Leu Pro Gly Met Asn Arg Pro Ile
 115 120 125
 Gln Val Lys Pro Ala Asp Ser Glu Ser Arg Gly Asp Arg Lys Leu Phe
 130 135 140
 Val Gly Met Leu Asn Lys Gln Gln Ser Glu Asp Val Arg Arg Leu
 145 150 155 160
 Phe Glu Ala Phe Gly Asn Ile Glu Glu Cys Thr Ile Leu Arg Gly Pro
 165 170 175
 Asp Gly Asn Ser Lys Gly Cys Ala Phe Val Lys Tyr Ser Ser His Ala
 180 185 190
 Glu Ala Gln Ala Ala Ile Asn Ala Leu His Gly Ser Gln Thr Met Pro
 195 200 205
 Gly Ala Ser Ser Ser Leu Val Val Lys Phe Ala Asp Thr Asp Lys Glu
 210 215 220
 Arg Thr Met Arg Arg Met Gln Gln Met Ala Gly Gln Met Gly Met Phe
 225 230 235 240
 Asn Pro Met Ala Ile Pro Phe Gly Ala Tyr Gly Ala Tyr Ala Gln Ala
 245 250 255
 Leu Met Gln Gln Gln Ala Ala Leu Met Ala Ser Val Ala Gln Gly Gly
 260 265 270
 Tyr Leu Asn Pro Met Ala Ala Phe Ala Ala Ala Gln Met Gln Gln Met

80

		275					280					285			
Ala	Ala	Leu	Asn	Met	Asn	Gly	Leu	Ala	Ala	Ala	Pro	Met	Thr	Pro	Thr
	290					295					300				
Ser	Gly	Gly	Ser	Thr	Pro	Pro	Gly	Ile	Thr	Ala	Pro	Ala	Val	Pro	Ser
305					310					315					320
Ile	Pro	Ser	Pro	Ile	Gly	Val	Asn	Gly	Phe	Thr	Gly	Leu	Pro	Pro	Gln
				325					330					335	
Ala	Asn	Gly	Gln	Pro	Ala	Ala	Glu	Ala	Val	Phe	Ala	Asn	Gly	Ile	His
			340					345					350		
Pro	Tyr	Pro	Ala	Gln	Ser	Pro	Thr	Ala	Ala	Asp	Pro	Leu	Gln	Gln	Ala
		355					360					365			
Tyr	Ala	Gly	Val	Gln	Gln	Tyr	Ala	Gly	Pro	Ala	Tyr	Pro	Ala	Ala	Tyr
	370					375					380				
Gly	Gln	Ile	Ser	Gln	Ala	Phe	Pro	Gln	Pro	Pro	Pro	Met	Ile	Pro	Gln
385					390					395					400
Gln	Gln	Arg	Glu	Gly	Pro	Glu	Gly	Cys	Asn	Leu	Phe	Ile	Tyr	His	Leu
			405						410					415	
Pro	Gln	Glu	Phe	Gly	Asp	Ala	Glu	Leu	Met	Gln	Met	Phe	Leu	Pro	Phe
			420					425					430		
Gly	Asn	Val	Ile	Ser	Ser	Lys	Val	Phe	Val	Asp	Arg	Ala	Thr	Asn	Gln
		435					440					445			
Ser	Lys	Cys	Phe	Gly	Phe	Val	Ser	Phe	Asp	Asn	Pro	Ala	Ser	Ala	Gln
	450					455					460				
Thr	Ala	Ile	Gln	Ala	Met	Asn	Gly	Phe	Gln	Ile	Gly	Met	Lys	Arg	Leu
465					470					475					480
Lys	Val	Gln	Leu	Lys	Arg	Pro	Lys	Asp	Ala	Asn	Arg	Pro	Tyr		
				485					490						

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<210> 235
<211> 826
<212> PRT
<213> Homo sapiens
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<400>	235															
Met	Glu	Gly	Ala	Gly	Gly	Ala	Asn	Asp	Lys	Lys	Lys	Ile	Ser	Ser	Glu	
				5					10					15		
Arg	Arg	Lys	Glu	Lys	Ser	Arg	Asp	Ala	Ala	Arg	Ser	Arg	Arg	Ser	Lys	
			20					25					30			
Glu	Ser	Glu	Val	Phe	Tyr	Glu	Leu	Ala	His	Gln	Leu	Pro	Leu	Pro	His	
		35					40					45				
Asn	Val	Ser	Ser	His	Leu	Asp	Lys	Ala	Ser	Val	Met	Arg	Leu	Thr	Ile	
	50					55					60					
Ser	Tyr	Leu	Arg	Val	Arg	Lys	Leu	Leu	Asp	Ala	Gly	Asp	Leu	Asp	Ile	
	65				70					75					80	
Glu	Asp	Asp	Met	Lys	Ala	Gln	Met	Asn	Cys	Phe	Tyr	Leu	Lys	Ala	Leu	
				85					90					95		
Asp	Gly	Phe	Val	Met	Val	Leu	Thr	Asp	Asp	Gly	Asp	Met	Ile	Tyr	Ile	
			100					105					110			
Ser	Asp	Asn	Val	Asn	Lys	Tyr	Met	Gly	Leu	Thr	Gln	Phe	Glu	Leu	Thr	
			115				120					125				
Gly	His	Ser	Val	Phe	Asp	Phe	Thr	His	Pro	Cys	Asp	His	Glu	Glu	Met	
	130					135					140					
Arg	Glu	Met	Leu	Thr	His	Arg	Asn	Gly	Leu	Val	Lys	Lys	Gly	Lys	Glu	
145					150					155					160	
Gln	Asn	Thr	Gln	Arg	Ser	Phe	Phe	Leu	Arg	Met	Lys	Cys	Thr	Leu	Thr	
				165					170					175		
Ser	Arg	Gly	Arg	Thr	Met	Asn	Ile	Lys	Ser	Ala	Thr	Trp	Lys	Val	Leu	
			180					185					190			

81

His	Cys	Thr	Gly	His	Ile	His	Val	Tyr	Asp	Thr	Asn	Ser	Asn	Gln	Pro
		195					200					205			
Gln	Cys	Gly	Tyr	Lys	Lys	Pro	Pro	Met	Thr	Cys	Leu	Val	Leu	Ile	Cys
	210					215					220				
Glu	Pro	Ile	Pro	His	Pro	Ser	Asn	Ile	Glu	Ile	Pro	Leu	Asp	Ser	Lys
225						230				235					240
Thr	Phe	Leu	Ser	Arg	His	Ser	Leu	Asp	Met	Lys	Phe	Ser	Tyr	Cys	Asp
				245					250					255	
Glu	Arg	Ile	Thr	Glu	Leu	Met	Gly	Tyr	Glu	Pro	Glu	Glu	Leu	Leu	Gly
			260					265					270		
Arg	Ser	Ile	Tyr	Glu	Tyr	Tyr	His	Ala	Leu	Asp	Ser	Asp	His	Leu	Thr
		275					280					285			
Lys	Thr	His	His	Asp	Met	Phe	Thr	Lys	Gly	Gln	Val	Thr	Thr	Gly	Gln
	290					295					300				
Tyr	Arg	Met	Leu	Ala	Lys	Arg	Gly	Gly	Tyr	Val	Trp	Val	Glu	Thr	Gln
305					310					315					320
Ala	Thr	Val	Ile	Tyr	Asn	Thr	Lys	Asn	Ser	Gln	Pro	Gln	Cys	Ile	Val
				325					330					335	
Cys	Val	Asn	Tyr	Val	Val	Ser	Gly	Ile	Ile	Gln	His	Asp	Leu	Ile	Phe
			340					345					350		
Ser	Leu	Gln	Gln	Thr	Glu	Cys	Val	Leu	Lys	Pro	Val	Glu	Ser	Ser	Asp
		355					360					365			
Met	Lys	Met	Thr	Gln	Leu	Phe	Thr	Lys	Val	Glu	Ser	Glu	Asp	Thr	Ser
	370					375					380				
Ser	Leu	Phe	Asp	Lys	Leu	Lys	Lys	Glu	Pro	Asp	Ala	Leu	Thr	Leu	Leu
385					390					395					400
Ala	Pro	Ala	Ala	Gly	Asp	Thr	Ile	Ile	Ser	Leu	Asp	Phe	Gly	Ser	Asn
				405					410					415	
Asp	Thr	Glu	Thr	Asp	Asp	Gln	Gln	Leu	Glu	Glu	Val	Pro	Leu	Tyr	Asn
		420						425					430		
Asp	Val	Met	Leu	Pro	Ser	Pro	Asn	Glu	Lys	Leu	Gln	Asn	Ile	Asn	Leu
		435					440					445			
Ala	Met	Ser	Pro	Leu	Pro	Thr	Ala	Glu	Thr	Pro	Lys	Pro	Leu	Arg	Ser
	450					455					460				
Ser	Ala	Asp	Pro	Ala	Leu	Asn	Gln	Glu	Val	Ala	Leu	Lys	Leu	Glu	Pro
465					470					475					480
Asn	Pro	Glu	Ser	Leu	Glu	Leu	Ser	Phe	Thr	Met	Pro	Gln	Ile	Gln	Asp
				485					490					495	
Gln	Thr	Pro	Ser	Pro	Ser	Asp	Gly	Ser	Thr	Arg	Gln	Ser	Ser	Pro	Glu
		500						505					510		
Pro	Asn	Ser	Pro	Ser	Glu	Tyr	Cys	Phe	Tyr	Val	Asp	Ser	Asp	Met	Val
	515						520					525			
Asn	Glu	Phe	Lys	Leu	Glu	Leu	Val	Glu	Lys	Leu	Phe	Ala	Glu	Asp	Thr
	530					535					540				
Glu	Ala	Lys	Asn	Pro	Phe	Ser	Thr	Gln	Asp	Thr	Asp	Leu	Asp	Leu	Glu
545					550					555					560
Met	Leu	Ala	Pro	Tyr	Ile	Pro	Met	Asp	Asp	Asp	Phe	Gln	Leu	Arg	Ser
				565					570					575	
Phe	Asp	Gln	Leu	Ser	Pro	Leu	Glu	Ser	Ser	Ser	Ala	Ser	Pro	Glu	Ser
			580					585					590		
Ala	Ser	Pro	Gln	Ser	Thr	Val	Thr	Val	Phe	Gln	Gln	Thr	Gln	Ile	Gln
		595					600					605			
Glu	Pro	Thr	Ala	Asn	Ala	Thr	Thr	Thr	Thr	Ala	Thr	Thr	Asp	Glu	Leu
	610					615					620				
Lys	Thr	Val	Thr	Lys	Asp	Arg	Met	Glu	Asp	Ile	Lys	Ile	Leu	Ile	Ala
625					630					635					640
Ser	Pro	Ser	Pro	Thr	His	Ile	His	Lys	Glu	Thr	Thr	Ser	Ala	Thr	Ser
				645					650					655	
Ser	Pro	Tyr	Arg	Asp	Thr	Gln	Ser	Arg	Thr	Ala	Ser	Pro	Asn	Arg	Ala

82

				660								670				
Gly	Lys	Gly	Val	Ile	Glu	Gln	Thr	Glu	Lys	Ser	His	Pro	Arg	Ser	Pro	
				675								685				
Asn	Val	Leu	Ser	Val	Ala	Leu	Ser	Gln	Arg	Thr	Thr	Val	Pro	Glu	Glu	
				690								700				
Glu	Leu	Asn	Pro	Lys	Ile	Leu	Ala	Leu	Gln	Asn	Ala	Gln	Arg	Lys	Arg	
705					710								715			
Lys	Met	Glu	His	Asp	Gly	Ser	Leu	Phe	Gln	Ala	Val	Gly	Ile	Gly	Thr	
				725								730				
Leu	Leu	Gln	Gln	Pro	Asp	Asp	His	Ala	Ala	Thr	Thr	Ser	Leu	Ser	Trp	
				740								745				
Lys	Arg	Val	Lys	Gly	Cys	Lys	Ser	Ser	Glu	Gln	Asn	Gly	Met	Glu	Gln	
				755								760				
Lys	Thr	Ile	Ile	Leu	Ile	Pro	Ser	Asp	Leu	Ala	Cys	Arg	Leu	Leu	Gly	
				770								775				
Gln	Ser	Met	Asp	Glu	Ser	Gly	Leu	Pro	Gln	Leu	Thr	Ser	Tyr	Asp	Cys	
785					790								795			
Glu	Val	Asn	Ala	Pro	Ile	Gln	Gly	Ser	Arg	Asn	Leu	Leu	Gln	Gly	Glu	
				805								810				
Glu	Leu	Leu	Arg	Ala	Leu	Asp	Gln	Val	Asn							
				820								825				

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<210> 236
<211> 342
<212> PRT
<213> Homo sapiens
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<400>	236															
Asn	Asn	Asn	Asn	Ser	Lys	His	Thr	Gly	His	Lys	Ser	Ala	Cys	Val	Pro	
				5					10					15		
Asn	Met	Thr	Glu	Arg	Arg	Arg	Asp	Glu	Leu	Ser	Glu	Glu	Ile	Asn	Asn	
			20					25					30			
Leu	Arg	Glu	Lys	Val	Met	Lys	Gln	Ser	Glu	Glu	Asn	Asn	Asn	Leu	Gln	
		35					40					45				
Ser	Gln	Val	Gln	Lys	Leu	Thr	Glu	Glu	Asn	Thr	Thr	Leu	Arg	Glu	Gln	
	50					55					60					
Val	Glu	Pro	Thr	Pro	Glu	Asp	Glu	Asp	Asp	Asp	Ile	Glu	Leu	Arg	Gly	
65					70				75						80	
Ala	Ala	Ala	Ala	Ala	Ala	Pro	Pro	Pro	Pro	Pro	Ile	Glu	Glu	Glu	Cys	Pro
				85					90						95	
Glu	Asp	Leu	Pro	Glu	Lys	Phe	Asp	Gly	Asn	Pro	Asp	Met	Leu	Ala	Pro	
			100					105					110			
Phe	Met	Ala	Gln	Cys	Gln	Ile	Phe	Met	Glu	Lys	Ser	Thr	Arg	Asp	Phe	
		115				120					125					
Ser	Val	Asp	Arg	Val	Arg	Val	Cys	Phe	Val	Thr	Ser	Met	Met	Thr	Gly	
	130					135					140					
Arg	Ala	Ala	Arg	Trp	Ala	Ser	Ala	Lys	Leu	Glu	Arg	Ser	His	Tyr	Leu	
145					150				155						160	
Met	His	Asn	Tyr	Pro	Ala	Phe	Met	Met	Glu	Met	Lys	His	Val	Phe	Glu	
				165					170					175		
Asp	Pro	Gln	Arg	Arg	Glu	Val	Ala	Lys	Arg	Lys	Ile	Arg	Arg	Leu	Arg	
		180						185					190			
Gln	Gly	Met	Gly	Ser	Val	Ile	Asp	Tyr	Ser	Asn	Ala	Phe	Gln	Met	Ile	
		195					200				205					
Ala	Gln	Asp	Leu	Asp	Trp	Asn	Glu	Pro	Ala	Leu	Ile	Asp	Gln	Tyr	His	
	210					215					220					
Glu	Gly	Leu	Ser	Asp	His	Ile	Gln	Glu	Glu	Leu	Ser	His	Leu	Glu	Val	
225					230					235					240	

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[illegible]

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<210> 237
<211> 403
<212> DNA
<213> Homo sapiens
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<400>	237						
ccagtgtggt	ggaattccag	cctcgtgccg	ggagtcgccg	catttgtggtc	cgcttctctg	60	
cactatgtcg	ggtggcctcc	tgaaggcgct	gcgcagcgac	tcctacgtgg	agctgagcca	120	
gtaccgggac	cagcacttcc	ggggtgacaa	tgaagaacaa	gaaaattac	tgaagaaaag	180	
ctgtacgtta	tatgttggaa	atctttcttt	ttacacaact	gaagaacaaa	tctatgaact	240	
cttcagcaaa	agtgtgtgca	taaagaaaaa	cattatgggt	ctggataaaa	tgaagaaaac	300	
agcatctgga	ttctgttttg	tggaatatta	ctcacgcga	gatgcggaaa	acgccatgcg	360	
gtacataaat	gggacgcgtc	tggatgaccg	aatcattcgc	aca		403	

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<210> 238
<211> 183
<212> DNA
<213> Homo sapiens
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<400>	238						
tattaatagt	aatcaattac	gggggtcatta	gttcatagcc	catatatgga	gttcgcggtt	60	
tacaactta	cggtaaatgg	ccgcgcctggc	tgaccgccca	acgacccccg	cccattgacg	120	
tcaataatga	cgtatgttcc	catagtaacg	ccaataggga	ctttccattg	acgtcaatgg	180	
gtg						183	

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<210> 239
<211> 403
<212> DNA
<213> Homo sapiens
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<400> 239						
ttttgatgct	ttctttcatg	ggaatagtca	ctttttttatt	tagtaaatcg	cattgctgga	60
accaccaagg	agtgtggaat	gtccttgagt	gtattattta	tgcaagtcac	agtcacgttg	120
ccatcatggc	agctatgtga	aacactaata	aatgtgtttt	tactttttat	tcccgttaaa	180
actgatgtaa	aacaggataa	aggcttgtta	tagtcactta	taagtatctg	ggtctaagta	240
atttccttag	atgtttctaa	agaaacattt	tcagctttgc	tcccattatg	attccaataa	300
ggaacgcttt	cctagtgcaa	ttttaggagt	aaagtttgaa	gagataaaaa	tagccaaaga	360
taggagacgt	ctgaattttg	aatgataaac	agtgatgttt	ttaa		403

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<210> 240
<211> 3148
<212> DNA
<213> Homo sapiens
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<400> 240

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aacttctcgg gaagatgagg cagtttggca tctgtggccg agttgctgtt gccgggtgat 60
agttggagcg gagacttagc ataatggcag aacctgttcc tccactgaag cactttgtgc 120
tggctaagaa ggcgattact gcagtccttg accagttact ggagtttgtt actgaaggat 180
cacattttgt tgaagcaaca tataagaatc cggaacttga tcgaatagcc actgaagatg 240
atctggtaga aatgcaagga tataaagaca agctttccat cattggtagg gtgctatctc 300
ggagacacat gaagggtggca ttttttggca ggacaagcag tgggaagagc tctgttatca 360
atgcaatgtt gtgggataaa gttctcccta gtgggattgg ccatataacc aattgcttcc 420
taagtgttga aggaactgat ggagataaag cctatccttat gacagaagga tcagatgaaa 480
aaaagagtggt gaagacagtt aatcaactgg cccatgccct tcacatggac aaagatttga 540
aagctggcgtg tcttgtacgt gtgttttggc caaaagcaaa atgtgccctc ttgagagatg 600
acctggtgtt agtagacagt gatgtccttg ttttggctgc aaactctgaa tcaacactaa 720
ataagttttg cctagatgct tttcacaagg tgaatgagcg gctttccaag cctaataatt 780
tgaatcagga aaaacacttt gatgcctctg catcagagcc agaatatatg gaagacgtac 840
tcattctcaa taatcgttgg tgccctgcatt tcttgggtga ggagctcaaa gttgtaaatg 900
gcagacagca catggaaaga atcttctttg tttcagcaaa ggaagttcctt agtgctagaa 960
ctttagaagc acagaatcgt ccagaaaagtg gtgtggcact tgctgaagga tttcatgcaa 1020
agcaaaaagc acaggggatg tttgaacaaa tctttgagga gtgtatctcg cagtcagcag 1080
gattacagga atttcagaat cactactatca gagctaaaca gatactagct actgtgaaaa 1140
tgaaaaacaa gttcgaacag ctggcagctg aagataaaaag gtttcatgtg caatgacaga 1200
acataatgga ttcagtaaac ttttgggtga tgaattttgt tcagagtttc atcctaattc 1260
tgaaatttgt agatgtatta aaaatatata aaagtgaatt aaataagcac atagaggatg gtatgggaag 1320
aaattttggt gatcgatgca ccgatgaagt aaacgcctta gtgcttcaga cccagcaaga 1380
aattattgaa aatttgaagc cattacttcc agctgggtata caggataaac tacatacact 1440
gatcccttgc aagaaatttg atctcagtta taatctaaat taccacaagt tatgttcaga 1500
ttttcaagag gatattgtat ttcgtttttc cctgggctgg tcttcccttg tacatcgatt 1560
tttgggccct agaaatgctc aaaggggtgct cctaggatta tcagagccta tctttcagct 1620
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atcacagaa gaactcatga ttacattagt aacaggattg gcgtccgtta catctagaac 1740
ttctatgggc atcattattg ttggaggagt gatttggaaa actataggct ggaaactcct 1800
atctgtttca ttaactatgt atggagcttt gtatctttat gaaagactga gctggaccac 1860
ccatgccaaag gagcgagcct ttaaacagca gtttgtaaac tatgcaactg aaaaactgag 1920
gatgattgtt agctccacga gtgcaaaactg cagtcaccaa gtaaaacaac aaatagctac 1980
cacttttgct cgcctgtgcc aacaagttga tattactcaa aaacagctgg aagaagaaat 2040
tgctagatta cccaaagaaa tagatcagtt ggagaaaata caaaacaatt caaagctcct 2100
aagaaaataa gctgttcaac ttgaaaatga gctggagaat tttactaagc agtttctacc 2160
ttcaagcaat gaagaatcct aacaatagag attgctttgg tgaccatgat aggaggaaac 2220
gaaacttgta agattggaac agttgttatt tttatgaaat tactttaaat atgaattgta 2280
ctaactgtac ctaaaatagca aagccctgtg tagattctgg taatgatctg tctcagggta 2340
tgtgtatttt tgaagagtgt tatgtcctta gttttaattt tgagtaaaga aaaggctaaa 2400
atcatgaatt agttacaagc aacagtacca acttatgtga cccctgaggg gtggggctgt 2460
gagctcttaa tttgtttttg attctgaaaa actctgcttc ctggcatcca ggagttagag 2520
attgagcctt tcatcttctt tctcaaaact agtttttgat gctttcttcc atgggaaatg 2580
tcactttttt atttagtaaa tcgcattgct ggaaccacca aggagtgtgg aatgtccttg 2640
agtgtattat ttatgcaagt cacagtcacg ttgccatcat ggcagctatg tgaaacacta 2700
ataaatgtgt ttttactttt tattcccggt aaaactgatg taaaacagga taaaggcttg 2760
ttatagtcac ttataagtat ctgggtctaa gtaatttccct tagatgtttc taaagaaaca 2820
ttttcagctt tgctcccatt atgattccaa taaggaacgc tttcctagtg caattttagg 2880
agtaaagttt gaagagataa aatatgccaa agataggaga cgtctgaatt ttgaatgata 2940
aacagtgatg ttttaaaaaa gctgttgttc ttcaggaggc atttgcctag gatattgctg 3000
gattataccc cattggaggc ttttaatttt atttgtatga attttccagg atttcattaa 3060
aaattattat tgtatttttt accttaatga aagattttgg gttcaaatat ctttctatat 3120
taaaagctga ttgagtctgt acatatgt 3148

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<210> 241

<211> 283

<212> DNA

<213> Homo sapiens

<400> 241

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ctctttgggt	cccactgttc	catttttatgc	taatagattc	cattctaggg	cccagccgtc	120
tcttgactga	tggtgttccc	tttaaccctt	ggcatgtata	atagaatttt	ggtgaatgaa	180
agaacccaaa	taggccagat	agtcacccca	ggccctgata	tccataaaaag	gcttgggaat	240
gcattatgta	attgtcctta	gtctttttgt	tgtttttagaa	aaa		283

<210> 242

<211> 5526

<212> DNA

<213> Homo sapiens

<400> 242

cgggccctgg	ggctcgggag	tcgggggagg	tgggacagtg	cggctactct	tgatcctctc	60
cggctgcttg	gtctacggca	cagctgaaac	tgatgtaaat	gtggtcatgc	ttcaggaatc	120
ccaagtttgt	gaaaagcgtg	ccagccaaca	attctgttac	acaaatgtgc	ttatcccaaa	180
atggcatgat	atatggacac	ggatacagat	ccgagtaaat	agttccagat	tggttcgagt	240
caccaggtg	gagaatgagg	agaaactgaa	ggagctagag	cagtttagta	tctggaactt	300
tttttctctc	tttttaaaag	agaaattgaa	tgacacctat	gttaacgtgg	gtctatacag	360
cacaaaaacc	tgcctcaaag	ttgagattat	agagaaggac	accaagtaca	gtgtcattgt	420
gatccggaga	tttgatccca	aactctttct	tgttttcctt	cttggaactta	tgctattttt	480
ttgtggagac	ttgctgagca	gaagtcaaat	tttctactac	tctactggga	tgactgtggg	540
aattgtggcc	tctctgtcaa	tcatcatttt	tatactatct	aagtttatgc	ctaagaaaag	600
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<211> 303

<212> DNA

<213> Homo sapiens

<400> 243

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87

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<210> 244
<211> 2393
<212> DNA
<213> Homo sapiens

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<210> 245
<211> 473
<212> DNA
<213> Homo sapiens

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88

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<210> 246

<211> 513

<212> DNA

<213> Homo sapiens

<400> 246

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<210> 247

<211> 533

<212> DNA

<213> Homo sapiens

<400> 247

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ttgatctttc accacagcag aaagagtggc agaggatgct gcagctgatt cagagtaggc 480
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<210> 248

<211> 1362

<212> DNA

<213> Homo sapiens

<400> 248

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89

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<210> 249

<211> 513

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

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<400> 249

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<210> 250

<211> 1172

<212> DNA

<213> Homo sapiens

<400> 250

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<210> 251

90

<211> 483
 <212> DNA
 <213> Homo sapiens

<400> 251
 atataccatt taatacattt acactttctt atttaagaag atattgaatg caaaataatt 60
 gacatataga actttacaaa catatgtcca aggactctaa attgagactc ttccacatgt 120
 acaatctcat catcctgaag cctataatga agaaaaagat ctagaaactg agttgtggag 180
 ctgactctaa tcaaagtga tgattggaat tagaccattt ggcctttgaa ctttcatagg 240
 aaaaatgacc caacatttct tagcatgagc tacctcatct ctagaagctg ggatggactt 300
 actattcttg tttatatattt agatactgaa aggtgctatg cttctgttat tattccaaga 360
 ctggagatag gcagggctaa aaaggtatta ttatttttcc tttaatgatg gtgctaaaat 420
 ttttcctata aaattcctta aaaataaaga tggtttaatc actaccattg tgaaaacata 480
 act 483

<210> 252
 <211> 156
 <212> PRT
 <213> Homo sapiens

<400> 252
 Met Ser Gly Gly Leu Leu Lys Ala Leu Arg Ser Asp Ser Tyr Val Glu
 5 10 15
 Leu Ser Gln Tyr Arg Asp Gln His Phe Arg Gly Asp Asn Glu Glu Gln
 20 25 30
 Glu Lys Leu Leu Lys Lys Ser Cys Thr Leu Tyr Val Gly Asn Leu Ser
 35 40 45
 Phe Tyr Thr Thr Glu Glu Gln Ile Tyr Glu Leu Phe Ser Lys Ser Gly
 50 55 60
 Asp Ile Lys Lys Ile Ile Met Gly Leu Asp Lys Met Lys Lys Thr Ala
 65 70 75 80
 Cys Gly Phe Cys Phe Val Glu Tyr Tyr Ser Arg Ala Asp Ala Glu Asn
 85 90 95
 Ala Met Arg Tyr Ile Asn Gly Thr Arg Leu Asp Asp Arg Ile Ile Arg
 100 105 110
 Thr Asp Trp Asp Ala Gly Phe Lys Glu Gly Arg Gln Tyr Gly Arg Gly
 115 120 125
 Arg Ser Gly Gly Gln Val Arg Asp Glu Tyr Arg Gln Asp Tyr Asp Ala
 130 135 140
 Gly Arg Gly Gly Tyr Gly Lys Leu Ala Gln Asn Gln
 145 150 155

<210> 253
 <211> 370
 <212> PRT
 <213> Homo sapiens

<400> 253
 Met Ala Glu Pro Val Ser Pro Leu Lys His Phe Val Leu Ala Lys Lys
 5 10 15
 Ala Ile Thr Ala Val Phe Asp Gln Leu Glu Phe Val Thr Glu Gly
 20 25 30
 Ser His Phe Val Glu Ala Thr Tyr Lys Asn Pro Glu Leu Asp Arg Ile
 35 40 45
 Ala Thr Glu Asp Asp Leu Val Glu Met Gln Gly Tyr Lys Asp Lys Leu
 50 55 60
 Ser Ile Ile Gly Glu Val Leu Ser Arg Arg His Met Lys Val Ala Phe
 65 70 75 80

91

[illegible]

<210> 254

<211> 429

<212> PRT

<213> Homo sapiens

<400> 254

Gly	Pro	Trp	Gly	Ser	Gly	Val	Gly	Gly	Gly	Gly	Thr	Val	Arg	Leu	Leu
				5					10					15	
Leu	Ile	Leu	Ser	Gly	Cys	Leu	Val	Tyr	Gly	Thr	Ala	Glu	Thr	Asp	Val
			20					25					30		
Asn	Val	Val	Met	Leu	Gln	Glu	Ser	Gln	Val	Cys	Glu	Lys	Arg	Ala	Ser
		35					40					45			
Gln	Gln	Phe	Cys	Tyr	Thr	Asn	Val	Leu	Ile	Pro	Lys	Trp	His	Asp	Ile
	50					55					60				
Trp	Thr	Arg	Ile	Gln	Ile	Arg	Val	Asn	Ser	Ser	Arg	Leu	Val	Arg	Val
	65				70					75				80	
Thr	Gln	Val	Glu	Asn	Glu	Glu	Lys	Leu	Lys	Glu	Leu	Glu	Gln	Phe	Ser
				85					90					95	
Ile	Trp	Asn	Phe	Phe	Ser	Ser	Phe	Leu	Lys	Glu	Lys	Leu	Asn	Asp	Thr

92

Tyr	Val	Asn	Val	Gly	Leu	Tyr	Ser	Thr	Lys	Thr	Cys	Leu	Lys	Val	Glu
		115					120					125			
Ile	Ile	Glu	Lys	Asp	Thr	Lys	Tyr	Ser	Val	Ile	Val	Ile	Arg	Arg	Phe
		130				135					140				
Asp	Pro	Lys	Leu	Phe	Leu	Val	Phe	Leu	Leu	Gly	Leu	Met	Leu	Phe	Phe
145					150					155					160
Cys	Gly	Asp	Leu	Leu	Ser	Arg	Ser	Gln	Ile	Phe	Tyr	Tyr	Ser	Thr	Gly
				165					170					175	
Met	Thr	Val	Gly	Ile	Val	Ala	Ser	Leu	Leu	Ile	Ile	Ile	Phe	Ile	Leu
			180					185					190		
Ser	Lys	Phe	Met	Pro	Lys	Lys	Ser	Pro	Ile	Tyr	Val	Ile	Leu	Val	Gly
		195					200					205			
Gly	Trp	Ser	Phe	Ser	Leu	Tyr	Leu	Ile	Gln	Leu	Val	Phe	Lys	Asn	Leu
		210				215					220				
Gln	Glu	Ile	Trp	Arg	Cys	Tyr	Trp	Gln	Tyr	Leu	Leu	Ser	Tyr	Val	Leu
225					230					235					240
Thr	Val	Gly	Phe	Met	Ser	Phe	Ala	Val	Cys	Tyr	Lys	Tyr	Gly	Pro	Leu
				245					250					255	
Glu	Asn	Glu	Arg	Ser	Ile	Asn	Leu	Leu	Thr	Trp	Thr	Leu	Gln	Leu	Met
			260					265					270		
Gly	Leu	Cys	Phe	Met	Tyr	Ser	Gly	Ile	Gln	Ile	Pro	His	Ile	Ala	Leu
		275					280					285			
Ala	Ile	Ile	Ile	Ile	Ala	Leu	Cys	Thr	Lys	Asn	Leu	Glu	His	Pro	Ile
		290				295					300				
Gln	Trp	Leu	Tyr	Ile	Thr	Cys	Arg	Lys	Val	Cys	Lys	Gly	Ala	Glu	Lys
305					310					315					320
Pro	Val	Pro	Pro	Arg	Leu	Leu	Thr	Glu	Glu	Glu	Tyr	Arg	Ile	Gln	Gly
				325					330					335	
Glu	Val	Glu	Thr	Arg	Lys	Ala	Leu	Glu	Glu	Leu	Arg	Glu	Phe	Cys	Asn
			340					345					350		
Ser	Pro	Asp	Cys	Ser	Ala	Trp	Lys	Thr	Val	Ser	Arg	Ile	Gln	Ser	Pro
		355					360					365			
Lys	Arg	Phe	Ala	Asp	Phe	Val	Glu	Gly	Ser	Ser	His	Leu	Thr	Pro	Asn
		370				375					380				
Glu	Val	Ser	Val	His	Glu	Gln	Glu	Tyr	Gly	Leu	Gly	Ser	Ile	Ile	Ala
385				390						395					400
Gln	Asp	Glu	Ile	Tyr	Glu	Glu	Ala	Ser	Ser	Glu	Glu	Glu	Asp	Ser	Tyr
				405					410					415	
Ser	Arg	Cys	Pro	Ala	Ile	Thr	Gln	Asn	Asn	Phe	Leu	Thr			
			420					425							

<210> 255

<211> 531

<212> PRT

<213> Homo sapiens

<400> 255

Met	Ser	Arg	Ser	Pro	Gln	Arg	Ala	Leu	Pro	Pro	Gly	Ala	Leu	Pro	Arg
				5					10					15	
Leu	Leu	Gln	Ala	Ala	Pro	Ala	Ala	Gln	Pro	Arg	Ala	Leu	Leu	Pro	Gln
			20					25					30		
Trp	Pro	Arg	Arg	Pro	Gly	Arg	Arg	Trp	Pro	Ala	Ser	Pro	Leu	Gly	Met
		35				40					45				
Lys	Val	Phe	Arg	Arg	Lys	Ala	Leu	Val	Leu	Cys	Ala	Gly	Tyr	Ala	Leu
	50				55						60				
Leu	Leu	Val	Leu	Thr	Met	Leu	Asn	Leu	Leu	Asp	Tyr	Lys	Trp	His	Lys
65					70					75					80

Glu	Pro	Leu	Gln	Gln	Cys	Asn	Pro	Asp	Gly	Pro	Leu	Gly	Ala	Ala	Ala
				85					90					95	
Gly	Ala	Ala	Gly	Gly	Lys	Leu	Gly	Ala	Pro	Arg	Ala	Ala	Ser	Gly	Arg
			100					105					110		
Ala	Ala	Pro	Cys	Ser	Cys	Pro	Phe	Gly	Pro	Pro	His	Ser	Leu	Pro	Pro
		115					120					125			
Ser	Arg	Cys	Arg	Arg	Arg	Gly	Asp	Thr	Leu	Gln	Pro	Arg	Gln	Gly	Trp
	130					135					140				
Arg	Gly	Leu	Arg	Pro	Leu	Gln	Ala	Met	Ala	Leu	Gly	Ala	Pro	Glu	Gly
145					150					155				160	
Val	Gly	Asp	Lys	Arg	His	Trp	Met	Tyr	Val	Phe	Thr	Thr	Trp	Arg	Ser
				165					170					175	
Gly	Ser	Ser	Phe	Phe	Gly	Glu	Leu	Phe	Asn	Gln	Asn	Pro	Glu	Val	Phe
			180					185					190		
Phe	Leu	Tyr	Glu	Pro	Val	Trp	His	Val	Trp	Gln	Lys	Leu	Tyr	Pro	Gly
		195					200					205			
Asp	Ala	Val	Ser	Leu	Gln	Gly	Ala	Ala	Arg	Asp	Met	Leu	Ser	Ala	Leu
	210					215					220				
Tyr	Arg	Cys	Asp	Leu	Ser	Val	Phe	Gln	Leu	Tyr	Ser	Pro	Ala	Gly	Ser
225					230					235					
Gly	Gly	Arg	Asn	Leu	Thr	Thr	Leu	Gly	Ile	Phe	Gly	Ala	Ala	Thr	Asn
				245					250					255	
Lys	Val	Val	Cys	Ser	Ser	Pro	Leu	Cys	Pro	Ala	Tyr	Arg	Lys	Glu	Val
			260					265					270		
Val	Gly	Leu	Val	Asp	Asp	Arg	Val	Cys	Lys	Lys	Cys	Pro	Pro	Gln	Arg
		275					280					285			
Leu	Ala	Arg	Phe	Glu	Glu	Glu	Cys	Arg	Lys	Tyr	Arg	Thr	Leu	Val	Ile
	290					295					300				
Lys	Gly	Val	Arg	Val	Phe	Asp	Val	Ala	Val	Leu	Ala	Pro	Leu	Leu	Arg
305					310					315					320
Asp	Pro	Ala	Leu	Asp	Leu	Lys	Val	Ile	His	Leu	Val	Arg	Asp	Pro	Arg
				325					330					335	
Ala	Val	Ala	Ser	Ser	Arg	Ile	Arg	Ser	Arg	His	Gly	Leu	Ile	Arg	Glu
			340					345					350		
Ser	Leu	Gln	Val	Val	Arg	Ser	Arg	Asp	Pro	Arg	Ala	His	Arg	Met	Pro
		355					360					365			
Phe	Leu	Glu	Ala	Ala	Gly	His	Lys	Leu	Gly	Ala	Lys	Lys	Glu	Gly	Val
	370				375						380				
Gly	Gly	Pro	Ala	Asp	Tyr	His	Ala	Leu	Gly	Ala	Met	Glu	Val	Ile	Cys
385					390					395					400
Asn	Ser	Met	Ala	Lys	Thr	Leu	Gln	Thr	Ala	Leu	Gln	Pro	Pro	Asp	Trp
				405					410					415	
Leu	Gln	Gly	His	Tyr	Leu	Val	Val	Arg	Tyr	Glu	Asp	Leu	Val	Gly	Asp
			420					425					430		
Pro	Val	Lys													

<210> 256
 <211> 378
 <212> PRT
 <213> Homo sapiens

<400> 256

Met	Arg	Arg	Leu	Asn	Arg	Lys	Lys	Thr	Leu	Ser	Leu	Val	Lys	Glu	Leu
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Asp	Ala	Phe	Pro	Lys	Val	Pro	Glu	Ser	Tyr	Val	Glu	Thr	Ser	Ala	Ser
			20					25					30		
Gly	Gly	Thr	Val	Ser	Leu	Ile	Ala	Phe	Thr	Thr	Met	Ala	Leu	Leu	Thr
		35					40					45			
Ile	Met	Glu	Phe	Ser	Val	Tyr	Gln	Asp	Thr	Trp	Met	Lys	Tyr	Glu	Tyr
	50					55					60				
Glu	Val	Asp	Lys	Asp	Phe	Ser	Ser	Lys	Leu	Arg	Ile	Asn	Ile	Asp	Ile
	65				70					75				80	
Thr	Val	Ala	Met	Lys	Cys	Gln	Tyr	Val	Gly	Ala	Asp	Val	Leu	Asp	Leu
				85					90					95	
Ala	Glu	Thr	Met	Val	Ala	Ser	Ala	Asp	Gly	Leu	Val	Tyr	Glu	Pro	Thr
			100					105					110		
Val	Phe	Asp	Leu	Ser	Pro	Gln	Gln	Lys	Glu	Trp	Gln	Arg	Met	Leu	Gln
	115						120					125			
Leu	Ile	Gln	Ser	Arg	Leu	Gln	Glu	Glu	His	Ser	Leu	Gln	Asp	Val	Ile
	130					135					140				
Phe	Lys	Ser	Ala	Phe	Lys	Ser	Thr	Ser	Thr	Ala	Leu	Pro	Pro	Arg	Glu
145					150					155					160
Asp	Asp	Ser	Ser	Gln	Ser	Pro	Asn	Ala	Cys	Arg	Ile	His	Gly	His	Leu
				165					170					175	
Tyr	Val	Asn	Lys	Val	Ala	Gly	Asn	Phe	His	Ile	Thr	Val	Gly	Lys	Ala
		180						185					190		
Ile	Pro	His	Pro	Arg	Gly	His	Ala	His	Leu	Gly	Ser	Thr	Cys	Gln	Pro
	195						200					205			
Trp	Asn	Leu	Thr	Ile	Phe	Ser	His	Arg	Ile	Asp	His	Leu	Ser	Phe	Gly
	210					215					220				
Glu	Leu	Val	Pro	Ala	Ile	Ile	Asn	Pro	Leu	Asp	Gly	Thr	Glu	Lys	Ile
225					230					235					240
Ala	Ile	Asp	His	Asn	Gln	Met	Phe	Gln	Tyr	Phe	Ile	Thr	Val	Val	Pro
				245					250					255	
Thr	Lys	Leu	His	Thr	Tyr	Lys	Ile	Ser	Ala	Asp	Thr	His	Gln	Phe	Ser
			260					265					270		
Val	Thr	Glu	Arg	Glu	Arg	Ile	Ile	Asn	His	Ala	Ala	Gly	Ser	His	Gly
	275						280					285			
Val	Ser	Gly	Ile	Phe	Met	Lys	Tyr	Asp	Leu	Ser	Ser	Leu	Met	Val	Thr
	290					295					300				
Val	Thr	Glu	Glu	His	Met	Pro	Phe	Trp	Gln	Phe	Phe	Val	Arg	Leu	Cys
305					310					315					320
Gly	Ile	Val	Gly	Gly	Ile	Phe	Ser	Thr	Thr	Gly	Met	Leu	His	Gly	Ile
			325						330					335	
Gly	Lys	Phe	Ile	Val	Glu	Ile	Ile	Cys	Cys	Arg	Phe	Arg	Leu	Gly	Ser
			340					345					350		
Tyr	Lys	Pro	Val	Asn	Ser	Val	Pro	Phe	Glu	Asp	Gly	His	Thr	Asp	Asn
		355					360					365			
His	Leu	Pro	Leu	Leu	Glu	Asn	Asn	Thr	His						
	370					375									

<210> 257
 <211> 98

95

<212> PRT

<213> Homo sapiens

<400> 257

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Met Asn Gln Thr Ala Ile Leu Ile Cys Cys Leu Ile Phe Leu Thr Leu
      5      10      15
Ser Gly Ile Gln Gly Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys
      20      25      30
Ile Ser Ile Ser Asn Gln Pro Val Asn Pro Arg Ser Leu Glu Lys Leu
      35      40      45
Glu Ile Ile Pro Ala Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala
      50      55      60
Thr Met Lys Lys Lys Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser Lys
      65      70      75      80
Ala Ile Lys Asn Leu Leu Lys Ala Val Ser Lys Glu Met Ser Lys Arg
      85      90      95
Ser Pro

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<210> 258

<211> 530

<212> DNA

<213> Homo sapiens

<400> 258

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gaattcggca cgagggctgg aggctgagat gcaggagctc gccatccagc tgcacaagcg 60
ctgcgaggag gtagaggcca cgcggggcca ggtgtgtcag gagcaggagc tgcgcgcct 120
ggtggagagc tgctgctgga gcaggaccgc gcccgcgagg acctccaggc ccggctgcgg 180
gagacgtggg ccctggcccg ggatgctgcc ctctctctgg accagctgcg agcctgtcaa 240
gctgagctgt catctcgagt gaggcaggac cagccccctg gtacagccac tctgggccta 300
gccgtccccc cagctgactc caagggtcgg caagcgtccc tgcaggccat gaggctcccc 360
gagctctcgg gagccctgga ggaccgtgtc cgtgagatgg ggcaagcact gtgcttagtg 420
accagagacc tggagaagct gcagggtgctg aacgggaaga agtggcggga gacctagcct 480
gcgggcccga tctgacgttg ggtgattggt ccaccctgaa gctgtgtgcc 530

```

<210> 259

<211> 349

<212> DNA

<213> Homo sapiens

<400> 259

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gaattcggca cgaggccagt tcagtctgca agcgccagct cctctcatgg ccggcttacc 60
caocgccttg ccaatgccca ggggcaaacc tcataccacc acttcagaa cactgatcat 120
gacaccaaac aatcaggtac gtggtcctct ggacccttc ccgctggtgg tccctgggaa 180
cagcatccga gctgtgatat gactagagg agattgatgg tcctttgaat tagaagagta 240
actttttgag tatttggcca ttggtgtgtt gttctaggaa atcctctctt ttttgtggtg 300
ttgaggtccc ccatgtatag tttcagcagc gaggacactg tggttcttg 349

```

<210> 260

<211> 509

<212> DNA

<213> Homo sapiens

<400> 260

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gaattcggca cgaggcaatc atggcgccac ctgtgagata ctgcatcccc ggogaacgtc 60
tgtgtaactt ggaggagggc agcccgggca gcggcaccta caccgcccac ggctacatct 120
tttcgtcgtt tgccggctgt ctgatgaaga gcagcgagaa tggcgcgctt ccagtgggtg 180
ctgtagttag agaaacagag tcccagttac tgccagatgt gggagctatt gtaacctgta 240
aggtctctag catcaattca cgctttgcca aagtacacat cctgtatgtg ggggtccatgc 300

```

96

```

ctcttaagaa ctcttttcga ggaactatcc gcaaggaaga tgtccgagca actgaaaaag 360
acaaggttga aatttataag agtttccgcc caggtgacat tgtcttggcc aaagtgatct 420
ccttaggtga tgcacagtcc aactacctgc taaccaccgc cgagaacgag ctgggagtg 480
tggtagccca cagtgaagtca ggtatccag 509

```

```

<210> 261
<211> 510
<212> DNA
<213> Homo sapiens

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<400> 261
gaattcggca cgaggtgcat gttgtgtgag gatccccggg cgcgcgcgtc gctcgggccc 60
cgccatggcc gtcacatca cgctcaaaac gctgcagcag cagaccttca agatccgcat 120
ggagcctgac gagacggtga aggtgctaaa ggagaagata gaagctgaga agggctcgtga 180
tgccttcccc gtggctggac agaaactcat ctatgccggc aagatcttga gtgacgatgt 240
ccctatcagg gactatcgca tcgatgagaa gaactttgtg gtcgtcatgg tgaccaagac 300
caaagccggc caggggtacct cagcaccccc agaggcctca cccacagctg cccagagtc 360
ctctacatcc ttcccgctg cccccacctc aggcattgtc catccccac ctgccgccag 420
agaggacaag agcccatcag aggaatccgc cccacgacg tccccagagt ctgtgtcagg 480
ctcttgttcc ctcttcaggt aacaaccggg 510

```

```

<210> 262
<211> 432
<212> DNA
<213> Homo sapiens

```

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<400> 262
gacatgtaat tcttatttat ttttcaccct caacaaggaa gaaaggtctc tccctcaatt 60
ctgctcttcc aatacttgag gataggcacc cctaaccctc cttcctccag ggaggcctca 120
gcatcagtgt ctgtggacgt agtctctgaa gagtgcttca gctgatggg aaggagaaac 180
tcaagacaga gatcctccta gggatggcgt cactttcctg ccaactttct cgttgcctct 240
ccttgaaagc agaagaagtg ccagccctca gcttccgtca gatcttgggc tcctagggcc 300
ttgtacaagt ccatggccct ctggttccag tccaggacgg ccaggcgga ttgggagcag 360
cccttatcca agccacctc agccaccttt ttgattattt tggaaaccaat cccttgacct 420
cgatattccg gc 432

```

```

<210> 263
<211> 614
<212> DNA
<213> Homo sapiens

```

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<400> 263
gaattcggca cgaggcgcag agttgtcgt actggagaag tccctgggac tgagtaagg 60
gaataaatac agtgctcagg gcgagcgaca gattocagtt cttcagacaa acaatgggcc 120
aagtctaaca ggattgacta ctatagcagc tcattctagtc aagcaagcca acaaaagaata 180
tttgctgggg agtactgcag aagaaaaagc aatcgttcag cagtgggttag aatacaggg 240
cactcaagta gatgggcact ccagtaaaaa tgacatccac aactgttga aggatcttaa 300
ttcatatctt gaagataaag tctaccttac aggggtataac tttacattag cagatatact 360
attgtactat ggacttcatc gctttatagt tgacctgaca gttcaagaaa aggagaaata 420
tcttaagtga tctcgttggt tttgtcacat tcagcattat ccaggcatca ggcaacatct 480
gtctagtgtt ggtcttcatc aagaacagac tatatactaa ttcccctaga aagctgtcca 540
tgccatacag aagatctatt aaaaaatgtt ttaaaatgga aaatgtactc ttagaaccac 600
aggacttaat ggta 614

```

```

<210> 264
<211> 336
<212> DNA
<213> Homo sapiens

```

97

<400> 264

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gaattcggca cgagggggcac aacagagccg ctccoctctc ctgccccgc caccgggacg 60
gagagcgccc gccggtgcat ttccggcgac acctogcagt cattcctgcg gcttgccgcg 120
ccttgtagac agccggggcc ttctgtagaa cgggtgcaggc ctggggtagt ctcctgtctg 180
gacagagaag agaaaaatgc aggacactgg ctcaagagtg cctttgcatt ggtttggcct 240
tggctaccca gcactgggtg cttctggtgg gaatatttgc tattgaaaag caagcaagcg 300
tgccgtccct ggctgcaggg ctgctctttt ggaagt 336

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<210> 265

<211> 487

<212> DNA

<213> Homo sapiens

<400> 265

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gaattcggca cgaggtgact gtgggaaact cgaaacaag ctcacatctt cctgtgggaa 60
accttctagc aacaggatga gtctgcagt gactgcagtt gccaccttcc tctatgcgga 120
ggtctttgtt gtgttgcttc tctgcattcc ctccatttct cctaaaagat ggcagaagat 180
tttcaagtcc cggctggtgg agttgttagt gtccataggc aacaccttct ttgtggttct 240
cattgtcatc cttgtgctgt tggctatcga tgccgtgcgc gaaattcggg agtatgatga 300
tgtgacggaa aaggtgaacc tccagaacaa tcccggggcc atggagcact tccacatgaa 360
gcttttccgt gccagagga atctctacat tgctggcttt tccttgctgc tgtccttcc 420
gcttagacgc ctggtgactc tcatttcgca gcaggccacg ctgctggcct ccaatgaagc 480
ctttaa 487

```

<210> 266

<211> 418

<212> DNA

<213> Homo sapiens

<400> 266

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gaattcggca cgaggccgtg acctgctagc tgagcagcgc ttcccggggc gcgtgctgcc 60
ctcgacttgg gacctgctgt tgcacatgaa caacgcgcgc tacttgccgc aggccgactt 120
tgccgcgcgc gcgcacctga cccgctgcgg ggtgctcggg gcgctgaggg agttgcgggc 180
gcacacgggtg ctggcggcct cgtgcgcgcg ccaccgcgcg tcgctgcgcg tgctggagcc 240
cttcgaggtg cgcacccgcc tgctgggctg ggacgaccgc gcgttctacc tggaggcgcg 300
ctttgtcagc ctgcgggacg gtttcgtgtg cgcgctgctg cgttccggc agcacctgct 360
gggcacctca cccgagcgcg tcgtgcagca cctgtgcaa cgcaaggtgg aaccct 418

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<210> 267

<211> 418

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(418)

<223> n = A,T,C or G

<400> 267

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gaattcggca cgaggctggc tcccaccctg gagttggctc aacagattga ggaagagacc 60
atcaagtttg ggaaccgct aggtatccgc actgtggctg tcattgggtg catctccaga 120
gaagaccagg gcttcaggct gcgcattggg tgtgagattg tgattgctcc cctgggcgtt 180
tgattgatgt gctggaaaac ccgtnccttg tgcttgaccg gctgtacctg tgtggttctg 240
gatgaggcag ataggatgat tgacatgggc tttgagccag atgtccagaa gatcctggag 300
cacatgcctt gtcagcaacc agaagccaa acacggatga agcttgagga cccctgagaa 360
aaatgcttgg ccaacttttg agtcgggaaa acattaagta cccgccaaa cagtcatt 418

```

<210> 268

<211> 266

<212> DNA

<213> Homo sapiens

<400> 268

```

gaattcggca cgagggcttc tcaactgagt cctactttta tgtcctgcct gtggtgagca 60
caaatgttga gcacatcaat ccccatTTTg tagacgaaga gacagagttg agtgacttgc 120
ccaaagacac agggccagtg aggagttgtg caggTTTgcc ctggcattaa aataataaac 180
attgaaattc agtcgattcc cctatggact cagttataga totcatcagt tgaaggaaga 240
gagatgcctt ttcctattca accttt                                     266

```

<210> 269)

<211> 235

<212> DNA

<213> Homo sapiens

<400> 269

```

gaattcggca cgagggctcc tgcagccttt tcgctgggac tgcgcgacac cgccccccga 60
ccgggtgccc gctgtgtgcc aggcgggtg ctgggcacgg tcccgcgagt gccctataag 120
gactgccagg caataatgaa ggTtctTTta ctgaaggatg cgaaggaaga tgactgtggc 180
caggatccgt atatcaggga attaggatta tatggacttg aagccacttt gatcc      235

```

<210> 270

<211> 386

<212> DNA

<213> Homo sapiens

<400> 270

```

gaattcggca cgaggggttc tcgcggggccg ccgggtgctg gtcaccgggg caggcaaagg 60
tatagggcgc ggcacggtcc aggcgctgca cgcgacgggc gcgcgggtgg tggctgtgag 120
ccggactcag gcgatcttg acagccttgt ccgcgagtg cccgggatag aaccctgtgt 180
cgtggacctg ggtgactggg aggccaccga gcgggcgctt gggcagcgtg ggccccgtgg 240
acctgctggg gaacaacgcc cgctgtcgcc ctgctgcagc ccttcctgga ggtcaccaag 300
gaggcctttg acagatcctt tgaggtgaac ctgcgtgcgg catccagtgt cacagattgt 360
ggcaggggct taatacccgg gagtcc                                     386

```

<210> 271

<211> 406

<212> DNA

<213> Homo sapiens

<400> 271

```

gaattcggca cgaggggctg ctggctggct aagtccctcc cgctcccggc tctcgcctca 60
ctaggagcgg ctctcgggtg agcgggacag ggcgaagcgg cctgcgccca cggagcgcg 120
gacactgccc ggaagggacc gccacccttg cccctcagc tgccactcg tgatttccag 180
cggcctccgc gcgcgcacga tgccctcggc caccagccac agcgggagcg gcagcaagtc 240
gtccggaccg ccaccgccgt cgggttcctc cgggagtgag gcggccgcgg gagccggggc 300
cgccgcgcgg gcttctagca ccccgcaacc ggcaccggcg ctgtccagac cgaggccatg 360
aagcagattc tcggggtgat cgacaagaaa cttcggaacc tggaga                                     406

```

<210> 272

<211> 365

<212> DNA

<213> Homo sapiens

<400> 272

```

gaattcggca cgaggctcgc ctcaactagga gcggctctcg gtgcagcggg acaggggcgaa 60
gcggcctgcg cccacggagc gcgcgacact gcccggaagg gaccgccacc cttgccccct 120
cagctgccca ctctgtattt ccagcggcct ccgcgcgcgc acgatgccct cggccaccag 180
ccacagcggg agcggcagca agtcgtccgg accgccaccg ccgtcggggt cctccgggag 240

```

99

tgaggcggcc gcgggagccg gggccgcgcg ccggtttcta gcaccccgca accggcaccg 300
 gcgctgtcca gaccgaggcc atgaagcaga ttctcggggg gatcgacaag aaacttcgga 360
 acctg 365

<210> 273

<211> 376

<212> DNA

<213> Homo sapiens

<400> 273

gaattcggca cgaggctttg gccactcaga gcccccgggc cgcgggtogtc gtacgcctga 60
 aggcgggtcg tgccggcgcc cgctctagtc tccgcctccg ctccaggccg tccctccggg 120
 cttctcaatg gtttcccggt ggcctctcaa tggttttccc ggccggccctt gcgccgacgc 180
 caggagactt ccggagcttg gtgacgtcac agagcgagct tttctaccca aatacgcggc 240
 gggggaatag gctcgagggc ggggagcagt gacaattgct aggcggagac agtgcaggga 300
 agagagacct tataaaggat caggactggc gggagggtatt taactgaag gaatatctgc 360
 ttcactgttg caacca 376

<210> 274

<211> 385

<212> DNA

<213> Homo sapiens

<400> 274

gaattcggca cgaggcttgg gtccgtcgtc gcttcggtgt ccctgtcggg cttcccagca 60
 gcggcctagc gggaaaagta aaagatgtct gaatatattc gggtaaccga agatgagaac 120
 gatgagccca ttgaaatacc atcggaagac gatgggacgg tgctgctctc cacggttaca 180
 gccagtttc caggggcgtg tgggcttcgc tacaggaatc cagtgtctca gtgtatgaga 240
 ggtgtccggc tggtagaagg aattctgcat gcccagatg ctggctgggg aaatctgggt 300
 tatgttgtca actatccaaa agataacaaa agaaaaatgg atgagacaga tgcttcatca 360
 gcagtgaag tgaaaagagc agtcc 385

<210> 275

<211> 395

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(395)

<223> n = A,T,C or G

<400> 275

gaattcggca cgagggggag cggagagcgg accccagaga gccctgagca gcccaccgc 60
 cgccgcgggc ctagttagca tcacaccccg ggaggagccg cagctgccgc agccggcccc 120
 agtcaccatc accgcaacca tgagcagcga ggccgagacc cagcagccgc ccgccgcccc 180
 ccccgccgcc ccgcacctca gcgcgcccga caccaagccc ggcactacgg gcagcggcgc 240
 aaggagcggg gggccgggcg gcctcacatt cggcgggggc ttgccggcgg ggacaaagaa 300
 agggcattcg caacgaaggg ttttgggaaa caagtaaaat gggttcaatt gtaagggaac 360
 cggatttttg ttttnattca accagggaaa ttgac 395

<210> 276

<211> 282

<212> DNA

<213> Homo sapiens

<400> 276

gaattcggca cgagggcagg ggtggtcctg gctggcattg cctgagccgg cagtgatgaa 60
 gtggggagct tgcccttgac aggtgggggc tggctggggc cttaatgtga aaagacagt 120

100

```
gcaggcagct ggagtagagc gagcccagca gccctaaaaa gctgccttca tggccatcta 180
gccccagttc agggcagcat ccatagccca caagccagcg tgggtggggc gggggtggtc 240
ccacagctgg gttccacctg aagagcctcc gtgcctcgga gc 282
```

<210> 277
 <211> 615
 <212> DNA
 <213> Homo sapiens

```
<400> 277
gaattcggca cgaggccggt cggcctgggc aacctgcgct gaagatgocg ggaaaactcc 60
gtagtgaocg tggtttgaa tcagacaccg caatgaaaaa aggggagaca ctgcgaaagc 120
aaaccgagga gaaagagaaa aaagagaagc caaaatctga taagactgaa gagatagcag 180
aagaggaaga aactgttttc cccaaagcta aacaagttaa aaagaaagca gagccttctg 240
aagttgacat gaattctcct aaatccaaaa aggcaaaaaa gaaagaggag ccatctcaaa 300
atgacatttc tcctaaaacc aaaagtttga gaaagaaaaa ggagccatt gaaaagaaag 360
tggtttcttc taaaaccaa aaagtgaaca aaaatgagga gccttctgag gaagaaatag 420
atgctcctaa gcccaagaag atgaagaag aaaaggaaat gaatggagaa actagagaga 480
aaagcccaa actgaagaat ggatttcctc atcctgaacc ggactgtaac ccagtgaaag 540
ctgccagtga agaaagtaac agtgagatag agcaggaaat cctgtggaac aaaaagaag 600
cgctttctct atttt 615
```

<210> 278
 <211> 316
 <212> DNA
 <213> Homo sapiens

```
<400> 278
gaattcggca cgaggagaaa gggaaaaaag gcgtaaagac agacatgaag caagtgggtt 60
tgcaaggaga ccagatccag attctgatga agatgaagat tatgagcgag agaggaggaa 120
aagaagtatg ggcggagctg ccattgcccc acccacttct ctggtagaga aagacaaaaga 180
gttaccocga gattttcctt atgaagaagg actcaagacc tcgatcacag tctttccaag 240
cagccctttc ttccccagt gtaccgaagg aaccaagaac agaccogaga atcttccacc 300
cggaccctta gcaaac 316
```

<210> 279
 <211> 393
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)... (393)
 <223> n = A,T,C or G

```
<400> 279
gaattcggca cgagggtgaa accaacttat tgggctcaat cccatttggt cacaggatac 60
tgtacgtatc ttcttttcca gagatttgat atcaccacaga caccgccagc atacataaac 120
gtgttaccag gtttgcccc gtaaccagc atatatacac ccttggccag cttttctcct 180
gaatatcagc taccagatc agtaccagtg gtgcctctt ttgtagcaa tgacagagca 240
gaaaaaaatg ctggctgcct attttgnngg gcattcattt tgaaatggct tgagaaatgg 300
ttggctgggt caccagaat tggccttctt gaaaaccaca agaatccctt tggaaggggg 360
cttctttttg gggaaaataa tcttggtaaa aag 393
```

<210> 280
 <211> 454
 <212> DNA
 <213> Homo sapiens

101

<400> 280

```

gaattcggca cgaggcagca atgcggtaga tatgacgtaa acaaattata attaagctag 60
tggtactca gagatcaaaa gaactgcaca ttgcattctg gagcatgaga aatcattttt 120
tttttcatga tgtctaactc tactgaattht attcaatgga gataacagaa agatgattat 180
atatgattaa attacttcca gtattagcag atgcttattt aaataacttg ttgttctttc 240
tgcaattcca catagaatta aggcaatagt ttaaaagaaa atttaaaaag taacttttct 300
agcattttta tgtagacctg tgaattctaa cacatttgca gtgtagccat cctaattgact 360
aaccagactt gaacaaaatc caacttgcaa aaacgatgca atataaatac caatcaccaa 420
taataggtag tctcactttt aaaaacctgt gtct 454

```

<210> 281

<211> 613

<212> DNA

<213> Homo sapiens

<400> 281

```

gaattcggca cgagggtgcgc tcttcgttgc ccagtttccg ctgagtggtc gcgctctccgc 60
ccccaccaca ccagtcccgc tgcattctcg gccgggctct aggcgccatg gctccccgcg 120
ggaggaagcg taaggctgag gccgcggtgg tcgccgtagc cgagaagcga gagaagctgg 180
cgaacggcgg ggagggaatg gaggagcgga ccgttggtat cgagcattgc actagctgac 240
gcgtctatgg gcgcaacgcc gcggccctga gccaggcgct gcgcctggag gccccagagc 300
ttccagtaaa ggtgaacccg acgaagcccc ggaggggagc cttcgaggtg acgctgctgc 360
gcccgagcgg cagcagtgcg gagctctgga ctgggattaa gaaggggccc ccacgcaaac 420
tcaaattccc tgagcctcaa gaggtggtgg aagagttgaa gaagtacctg tcgtagggag 480
atttgggtag aagccctcat gctgagcttt gtgtccctgg tgatgttgga acattaatga 540
tggaacatgg ccaaaactca gtcattgatcc tgaagccatg gtttcttccc tgccagaaat 600
gaaggttcat tat 613

```

<210> 282

<211> 313

<212> DNA

<213> Homo sapiens

<400> 282

```

gaattcggca cgaggcgaga acgggcacgg ggagcagcag cctcaaccgc cggcgacgca 60
gcagcaacag ccccaacagc agcgcggggc cgccaaggag gccgcgggga agagcagcgg 120
ccccacctcg ctgttcgcgg tgacggtggc gccgccggg gcgaggcagg gccagcagca 180
ggcgggaggt aagaagaagg cggaaggcgg cggaggcggc ggtcgccccg gggctccggc 240
ggcgggggac ggcaaaacag aacagaaagg cggagataaa aagaggggtg ttaaaagacc 300
accacaagat cat 313

```

<210> 283

<211> 557

<212> DNA

<213> Homo sapiens

<400> 283

```

gaattcggca cgaggcctgg ccggggagac gagttgcatg tggttggttca gctggcgata 60
gcggcgggag cggagccggc ggggcctgtg cgaccgcctg ggtttgtgaa atggctgctg 120
acatttctga atccagcggg gctgactgca aaggagaccc aaggaacagt gccaggttag 180
atgccgatta cccacttcca gtcctttatt gtggagtctg ttcattacca acagagtact 240
gtgaatatat gcctgatgtt gctaaatgta gacaatgggt agagaagaat tttccaaatg 300
aatttgcaaa acttactgta gaaaattcac ccaacaaga agctggaatt agtgagggtc 360
aaggaacagc aggggaagaa gaggagaaga aaaaacagaa gagaggtgga aggggtcaaa 420
taaaacaaaa aaagaagacc gtaccacaaa aggttactat agccaaaatt cccagagcaa 480
agaagaaata tgtgacaaga gtatgtggcc ttgcaacttt tgaaattgat cttaaagaag 540
cacaagatt ttttgct 557

```

<210> 284

102

<211> 627
 <212> DNA
 <213> Homo sapiens

<400> 284
 gaattcggca cgaggctcac taggagcggc tctcgggtgca gcgggacagg gcgaagcggc 60
 ctgcgcccac ggagcgcgcg aactgcccg gaagggaccg ccacccttgc cccctcagct 120
 gccactcgt gatttccagc ggcctccgcg cgcgcacgat gccctcggcc accagccaca 180
 gcgggagcgg cagcaagtgc tccggaccgc caccgccgtc gggttcctcc gggagtggagg 240
 cggccgcggg agccggggcc gccgcgcggg cttctcagca ccccgcaacc ggcaccggcg 300
 ctgtccagac cgaggccatg aagcagattc tcgggggtgat cgacaagaaa cttcgggaacc 360
 tggagaagaa aaagggttaag cttgatgatt accaggaacg aatgaacaaa ggggaaaggc 420
 ttaatcaaga tcagctggat gccgtttcta agtaccagga agtcacaaat aatttggagt 480
 ttgcaaaaaga attacagagg agtttcatgg cactaagtca agatattcag aaaacaataa 540
 agaagacagc acgtcgggag cagcttatga aaaaagaact gaacagaaac gtttaaaaac 600
 ttgtacttga actacagtat tgttttgg 627

<210> 285
 <211> 474
 <212> DNA
 <213> Homo sapiens

<400> 285
 gaattcggca cgagggcgag aacgaccccc ggaccgacca aagcccgcg cccgctgcat 60
 cccgcgtcca gcacctacgt cccgctgccg tcgccgccgc caccatgccc aagagaaagg 120
 ctgaagggga tgctaaggga gataaagcaa aggtgaagga cgaaccacag agaagatccg 180
 cgaggttgct tgctaaacct gctcctccaa agccagagcc caagcctaaa aaggccccctg 240
 caaagaaggg agagaaggta cccaaaggga aaaagggaaa agctgatgct ggcaaggagg 300
 ggaataaccc tgcagaaaat ggagatgcc aacagacca ggacagaaa gctgaagggtg 360
 ctggagatgc caagtgaagt gtgtgcattt ttgataactg tgtacttctg gtgactgtac 420
 agtttgaaat actatTTTTT atcaagtttt ataaaaatgc agaatttttg tttta 474

<210> 286
 <211> 576
 <212> DNA
 <213> Homo sapiens

<400> 286
 gaattcggca cgaggggaat ctgtgaagct cactactgga ccaaacaacg ctggagctca 60
 aagtagttct tcatgtggga cttctggcct tcagtttct gcacagacag ccttggcaga 120
 acaacagcca aaaagcatga aaagcccagc ttctccagag cctggtttct gtgctactct 180
 ttgccctatg gtagaaattc caccataaga tataatggca gaattggagt cagaggatat 240
 cttgatccct gaagaatctg taattcagga ggaaattgca gaagaggtag agactagtat 300
 ctgtgaatgc caggatgaaa atcataagac aatacctgaa ttttctgagg aggctgaaag 360
 totaaccaat tctcatgaag aaccccaaat agcacctcct gaagataact tggaaacctg 420
 tggtatgatg aatgatgttt tagaaacttt gcctcatatt gaagttaaga tagaaggga 480
 gtcagaatca cccaggaag aaatgacagt tggtatcgat cagttagaag tctgtgactc 540
 tcttattcct tccacttcat ctatgactca tgtcag 576

<210> 287
 <211> 514
 <212> DNA
 <213> Homo sapiens

<400> 287
 gaattcggca cgaggcagag aggtttgcc aagagcgcag gctgagaata tggagagact 60
 atgtggctcc cacagctaatt ttggacaaaa aggacaagca gtttgttgcc aagggtgatgc 120
 aggttctgaa tgctgatgcc attgttgtga agctgaactc aggcgattac aagacgattc 180
 acctgtccag catccgacca ccgaggctgg agggggagaa caccaggat aagaacaaga 240

103

```

aactgcgtcc cctgtatgac attccttaca tgtttgaggg ccggaattt cttcgaaaaa 300
agcttatttg gaagaaggtc aatgtgacgg tggactacat tagaccagcc agcccagcca 360
cagagacagt gcctgccttt tcagagcgta cctgtgccac tgtcaccatt ggaggaataa 420
acattgctga ggctcttgtc agcaaaggtc tagccacagt gatcagatac cggcaggatg 480
atgaccagag atcatcacac tacgatgaac tgct                                     514

```

<210> 288

<211> 456

<212> DNA

<213> Homo sapiens

<400> 288

```

gaattcggca cgagggggcg ggcaggcggg caggccggca ggcgggtgcg cggaggggctg 60
gtgccccgca gcagggtgggc ggggtgcggt tggcggcggc ggctgggccc ggggctgccg 120
gctgcgctcg ggccgtgcgc ggcggccgtg cgggcacgcc atggacttca acatgaagaa 180
gctggcgctcg gacgcgggca tcttcttcac ccgggcggtg cagtccacgg aggagaaatt 240
tggccaggct gagaagactg agcttgatgc ccactttgaa aaccttctgg cccgggcaga 300
cagcaccaag aactggacag agaagatctt gaggcagaca gaggtgctgc tgcagcccaa 360
cccagtgccc cgagtggagg agttcctgta tgagaagctg gacaggaagg tcccctcaag 420
ggtcaccaac ggggagctgc tggctcagta catggc                                     456

```

<210> 289

<211> 262

<212> DNA

<213> Homo sapiens

<400> 289

```

gaattcggca cgaggcagaa gccctagct cctctgagcc tcatggggcc agaggaagca 60
gtagttcggg cggcaagaaa tgctacaagc tggagaatga gaagctgttc gaagagttcc 120
ttgaactttg taagatgcag acagcagacc accctgaggt ggtcccatcc ctctataacc 180
ggcagcaacg tgcccactct ctgttttttg cctcggcgga gttctgcaac atcctctcta 240
gggtcctgtc tcgggcccgg ac                                     262

```

<210> 290

<211> 205

<212> DNA

<213> Homo sapiens

<400> 290

```

gaattcggca cgaggattta tgggccactg cacatgcccg ctgcagccct gggatcagct 60
ggaagctgcc tgtcatctcc tgcccaatcc ccagaaaccc tgattcaggt ctgcaggctc 120
ctgcgggctc accaggctgc tggctccggt accatgtaaa cctaggaagg taaaggagca 180
ggcaacctcc tcgtggcctg tgtgt                                     205

```

<210> 291

<211> 483

<212> DNA

<213> Homo sapiens

<400> 291

```

gaattcggca cgaggcctgg ccgggaccgt gtgggcccgtg aggatgagga cggctgggag 60
acgcgagggg accgcaaggc ccggaagccc ctggtggaga agaagcggcg cgcgcggatc 120
aacgagagcc tgcaggagct gcggtgctg ctggcgggcg ccgaggtgca ggccaagctg 180
gagaacgcgc aagtgtctga gctgacgggt cggcgggtcc aggtgtgct gcggggccgg 240
gcgcgcgagc gcgagcagct gcaggcggaa gcgagcgaac gcttcgctgc cggctacatc 300
cagtgcattc acgaggtgca cacgttcgtg tccacgtgcc aggccatcga cgctaccgtt 360
ctgcgcgagc cctgaacat ctgctcgagt ccatgcgcgt gcgtgagggc agcaacttca 420
ggatctgctg ggggacgccc tgcggggcca cctaaatccc ctggacggaa tggctggctg 480
-cgg

```

104

<210> 292
 <211> 562
 <212> DNA
 <213> Homo sapiens

<400> 292
 gaattcggca cgagggcgct gcggttagga gccgggttgc gggagacccc aggttcggtt 60
 gggattccca gccagaacgg agcttaagcc gggcaggcga gcgaatgacg gagtagcgag 120
 ctgcacggcg gcgtgctgcg ctgttgagga cgctgtcccg cgcgctccca ggccgccccg 180
 aggcttgggg tcttcgaagg ataatcggcg cccggggccg aacagcgggg gcacacgggg 240
 cgctgccgaa gtgcaaggcc acggccagag ctcgagcccg acgcgctgtc tggagtcgta 300
 gggttgccgc gtttggggtc ggggtctgag gcttgggcgc tgcctggggc gagcgagat 360
 cggggtttgc ctcccgtccc cgctcaggac cctgacgtgg ctgaagcggc cccgggagca 420
 tgagcggcag cgcgtggacg tcaaggtggt gatgctgggc aaggagtacg tgggcaagac 480
 tagcctggtg gagcgctacg tgcacgaccg ctttctggtg gggccttatc agaacacccat 540
 cggggccgccc ttcgtggcca ag 562

<210> 293
 <211> 645
 <212> DNA
 <213> Homo sapiens

<400> 293
 gaattcggca cgaggctgag agagagcaca gcctggtggg ttctggggtc tacggcctag 60
 gggccgggga agtttgcgcc gccgcgacca gtgctgcgat cccgagccgg gctccagccc 120
 cgaggaccag gggctcggcg ggcctgccta cggaaccccg cgggccagca gcagtcgtct 180
 cgcgtcctcc tgcttggaag agtggtttaag cttctaaaat gtcattctatc aagcacctgg 240
 tttatgcagt tattcgtttc ttacgggaac aaagtcagat ggacacttac acctcggtatg 300
 aacaagaag tttggaagtt gcaattcagt gcttggagac agtttttaag atcagcccag 360
 aagatacaca cctagcagtt tcacagcctt tgacagaaat gtttaccagt tccttctgta 420
 agaatgacgt tctgcccctt tcaaaactcag tgctgaaga tgggggaaaa gctgaccaat 480
 taaaagatga aggcaataac cacatgaaag aagaaaatta tgctgctgca gtggattggt 540
 acacacaggc aatagaattg gatccaata atgcagttta ctattgcaac agggctgctg 600
 ctcagagcaa attaggtcac tacacagatg cgataaagga ttgtg 645

<210> 294
 <211> 521
 <212> DNA
 <213> Homo sapiens

<400> 294
 ctgagcgtct ctgcttagcc gcggtcatga gccggcacag ccggctgcag aggcaggttc 60
 tgagcctgta ccgcgatctg ctgcgcgccg ggcgtgggaa gccgggcgcc gaggcgcgag 120
 tgccggcaga gttccggcag catgcgggcc tgccgcggtc cgacgtgctg cgcacgagt 180
 acctgtaccg ccgcggggcg cgccagctgc agctgctacg ctccggccac gccaccgcca 240
 tgggcgcctt cgtacgcccg cgggccccga ccggggagcc tggcggcgtg ggttcccagc 300
 ctgacgacgg cgacagtcca aggaaccccc acgacagcac gggggcaccg gagaccgccc 360
 ccgacggacg gtgacaggcg aagagccgaa ctgcgtcgat ggcgtggtgg agccaggagg 420
 ctgcctgac tgcattgggg gactggggaa cccgcctaag gtgagaggtc ttaagagact 480
 agcttgacga attggggatg tcagagactc ctccctggcg a 521

<210> 295
 <211> 375
 <212> DNA
 <213> Homo sapiens

<400> 295
 gaattcggca cgaggagAAC atgcagtcta ggaaccggca tgcgcataac ctcaggatat 60

105

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aaataatgct gaagcagagt tacgtttttt ttgtttgtgt tttttttgtt tttgtttttt 120
taggtttccg tgtgtttcta ttgagctgct cagtgcccg cttagaagac caggaaaagg 180
agtcacaggt cgtatgctgg aggcttgagc cgcggcaccg tggcgcggt cgcctcgtg 240
cggttggtgg tggcggtgga cattgcagcg cggctggagg gggtccttag acaaggtgca 300
agacaaacag aagagggcac gtggggtcaa actcctactg cctgcctgat tttctgccac 360
aggacaaatt cacca                                     375

```

<210> 296

<211> 628

<212> DNA

<213> Homo sapiens

<400> 296

```

gaattcggca cgaggaaaat ggttcgctat tcacttgacc cggagaaccc cacgaaatca 60
tgcaaatcaa gaggttccaa tcttcgtgtt cactttaaga acactcgtga aactgctcag 120
gccatcaagg gtatgcatat acgaaaagcc acgaagtatc tgaaagatgt cactttacag 180
aaacagtgtg taccattccg acgttacaat ggtggagttg gcaggtgtgc gcaggccaag 240
caatggggct ggacacaagg tcggtggccc aaaaagagtg ctgaattttt gctgcacatg 300
cttaaaaacg cagagagtaa tgctgaactt aagggttttag atgtagattc tctggtcatt 360
gagcatatcc aagtgaacaa agcacctaag atgcgcgcgc ggacctacag agctcatggt 420
cggattaacc catacatgag ctctccctgc cacattgaga tgatccttac ggaaaaggaa 480
cagattgttc ctaaaccaga agaggagggt gccagaaga aaaagatatc ccagaagaaa 540
ctgaagaaac caaaacttat ggcacgggag taaatttctc ttaaaataaa tgtaattaaa 600
aggaaaaaaa aaaaaaaaaa aactcgag                                     628

```

<210> 297

<211> 645

<212> DNA

<213> Homo sapiens

<400> 297

```

gaattcggca cgaggagaaa acgaagcagc gttggaaaat ggaattaaaa atgaggaaaa 60
cacagaacca ggtgctgaat cttctgagaa cgctgatgat cccaacaaag atacaagtga 120
aaacgcagat ggtcaaagt atgagaacaa ggacgactat acaatcccag atgagtatag 180
aattggacca tatcagccca atgttcctgt tggatatagac tatgtgatac ctaaaacagg 240
gttttactgt aagctgtgtt cactotttta taaaaatgaa gaagttgcaa agaatactca 300
ttgcagcagc cttcctcatt atcagaaatt aaagaaattt ctgaataaat tggcagaaga 360
acgcagacag aagaaggaaa cttaagatgt gcaaggagat ttaatgattt caaagaaaat 420
aatggttctt tgtttttaat gttaaccttt tttaaataca atactgatag ttagaagaaa 480
actattgtac tcttttgttt tagtggagaa ataatagatg tctgttcatt tgtaagtgt 540
tatagcaaaa aaaatacaca tatggttaag ttaatgaata gtttttgttt tatcagaatg 600
gcaacagaca gaagtacttt gtagagattg acttcctaag ctctt                                     645

```

<210> 298

<211> 625

<212> DNA

<213> Homo sapiens

<400> 298

```

gaattcggca cgaggggatt cagcagcctc ccccttgagc cccctcgctt cccgacgttc 60
cgttccccc tgcccgctt ctcccgccac cgcgcgcgc gccttcgcga ggccgtttcc 120
accgaggaaa aggaatcgta tcgtatgtcc gctatccaga acctccactc ttctgacccc 180
tttgctgatg caagtaaggg tgatgacctg cttoctgctg gcaactgagga ttatatccat 240
ataagaattc aacagagaaa cggcaggaag acccttacta ctgtccaagg gatcgctgat 300
gattacgata aaaagaaact agtgaaggcg ttttaagaaaa agtttgcttg caatggtact 360
gtaattgagc atccggaata tggagaagta attcagctac agggtgacca acgcaagaac 420
atatgccagt tcctcgtaga gattggactg gctaaggacg atcagctgaa ggttcatggg 480
ttttaagtgc ttgtggctca ctgaagctta agtgaggatt tccttgcaat gagtagaatt 540
tcccttctct tccttgtcac aggttttaaaa acctcacagc ttgtataatg taaccatttg 600

```

106

gggtccgctt ttaacttgga ctagt

625

<210> 299

<211> 545

<212> DNA

<213> Homo sapiens

<400> 299

```

gaattcggca cgagggagcc caggaggtca aggctacagt gagccgtgat catgccactg 60
cactccagcc tgggtgacag agcgagaccc tgtctcttaa caacaaaacc catgagcggc 120
agccccccag tcctggatgg tggtaaagaa tcctcaagat caaaccacag cagtgtctgag 180
agcttggcct gattctaggg ctggggctgg agaaactgct agagatgatg ccgatagcca 240
gtgtgatccc cctgccctga tggcaaggc cagagtgcag actggaaccc tcccctcccc 300
aaagattcag acctgtggg ctgagtgggc tcatagtgtc ccaagtcct gagaggctgg 360
tgtctggctt cagcctccag cttctcaggt tctgatgcag tcagctgagt tccctgccta 420
ttcttgcaag cactaggagg aagggtggtg ggttgctggg aacagcaccg agcgccctcc 480
ccaccagat tcacagagca cactccccg ggggatactt taatccggag gccgtgacgc 540
ctgct

```

<210> 300

<211> 605

<212> DNA

<213> Homo sapiens

<400> 300

```

gaattgggca cgaggcgggc cgcagctttt cggttcacag cgggcaggga aagccgcggg 60
aagggtactc caggcgagag gcggacgcga gtcgtcgtgg caggaaaagt gactagctcc 120
ccttcgttgt cagccaggga cgagaacaca gccacgtccc cacccgctg ccaacgatcc 180
ctcggcggcg atgtcggccg ccggtgcccg aggcctgcgg gccacctacc accggctcct 240
cgataaagtg gagctgatgc tgcccagaaa attgaggccg ttgtacaacc atccagcagg 300
tcccagaaca gtttttttct gggctccaat tatgaaatgg gggttggtgt gtgctggatt 360
ggctgatatg gccagacctg cagaaaaact tagcacagct caatctgctg ttttgatggc 420
tacagggttt atttggtcaa gatactcact tgtaattatt ccaaaaaatt ggagtctgtt 480
tgctgttaat ttctttgtgg gggcagcagg agcctctcag ctttttctga tttggagata 540
taaccaagac taaaagctaa agcacacaaa taaaagagtt ctgatcacct gaacaatcta 600
gatgt

```

<210> 301

<211> 364

<212> DNA

<213> Homo sapiens

<400> 301

```

gaattcggca cgaggcgcac acgagaacat gcctctcgca aaggatctcc ttcatccctc 60
tccagaagag gagaagagga aacacaagaa gaaacgcctg gtgcagagcc ccaattccta 120
cttcatggat gtgaaatgcc caggatgcta taaaatcacc acggtcttta gccatgcaca 180
aacggtagtt ttgtgtgttg gctgctccac tgtcctctgc cagcctacag gaggaaaagc 240
aaggcttaca gaaggatgtt cttcaggag gaagcagcac taaaagcact ctgagtcaag 300
atgagtggga aaccatctca ataaacacat tttggataaa aaaaaaaaaa aaaaaaaact 360
cgag

```

<210> 302

<211> 545

<212> DNA

<213> Homo sapiens

<400> 302

```

gaattccggc acgaggggac cccagagagc cctgagcagc cccaccgcgg ccgcccgcct 60
agttaccatc acaccccgga aggagccgca gctgccgcag ccggccccag tcaccatcac 120

```

107

```

cgcaaccatg agcagcgagg cagagaccca gcagccgccc gccgcccccc ccgcccggcc 180
cgccctcagc gccgcccaga ccaagcccgg cactacgggc agcggcgagc ggagcgggtg 240
cccgggaggc ctcacatcgg cggcgccctg cggcggggac aagaaggcca tcgcaacgaa 300
ggttttggga acagtaaaat ggttcaatgt aaggaacgga tatggtttca tcaacaggaa 360
tgacaccaag gaagatgtat ttgtacacca gactgccata aagaagaata accccaggaa 420
gtaccttcgc agtgtaggag atggagagac tgtggagttt gatgttggtg aaggagaaaa 480
gggtgcggag gcagcaaatg ttacaggtcc tgggtggtgt ccagttcaag gcagtaataa 540
tgag                                     545

```

<210> 303

<211> 506

<212> DNA

<213> Homo sapiens

<400> 303

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gaattcggca cgaggctggt cactccgcca ccgtagaatc gcctaccatt tgggtgcaagc 60
aaaaagcaat cagcaattgg acaggaanaa aatggcattg aagcagattt ccagcaacaa 120
gtgctttggg ggattgcaga aagtttttga acatgacagt gttgaactaa actgcaaaaat 180
gaaatttgct gtctacttac caccaaaagg agaaaacagg aagtgccttg cactgtattg 240
gctctcaggt ttaacttgca cagagcaaaa ttttatatca aaatctgggt atcatcagtc 300
tgcttcagaa catggtcttg ttgtcattgc tccagatacc agccctctg gctgcaatat 360
taaagggtgaa gatgagagct gggactttgg cactggtgct ggattttatg ttgatgccac 420
tgaagatcct tggaaaacca actacagaat gtactcttat gtcacagagg agcttcccca 480
actcataaat gccaattttc cagtgg                                     506

```

<210> 304

<211> 485

<212> DNA

<213> Homo sapiens

<400> 304

```

gaattcggca cgagggagtt gtggggccag gagccctgag gctgccggca ggtgaactga 60
gtgcccagca gctgagacgg gcgcccaccc gtcctgagca tagctctgta ggcagtgcgg 120
gcatagcctg catagtgtcc tggcgctggg agttccccgt ggacagagcc agagggcagc 180
ggcgctccct gtcagagctg gatcaggccc cccatcgagg agggagggca gacggaggcc 240
cgagagcctc cccaggcctc ttcgtgggaa ggccccagta ccactcgtag gaggtctcag 300
ctctggcatg gctgccccgg atgtggccga gggggcttca ccctgtgtcc ttaggagggg 360
gtggccttga ggcaagagcc gtgcctcact gacccccagg ggccatcc tccccatgga 420
atgggctgta tgtcctgccc caacttgccc cgcagcaggc cagaccccccc taccgccgcc 480
cagag                                     485

```

<210> 305

<211> 615

<212> DNA

<213> Homo sapiens

<400> 305

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gaattcggca cgaggcttac aaggaaaatg ctgacttatg accggcgctc tgagcctcag 60
gttggggagc gagtgcata cgtcatcatt tatgggaccc ccggagtacc acttatccag 120
cttgtaaggc gccagtgga agtcctgcag gacccaactc tgagactgaa tgctacttac 180
tatattacca agcaaatcct tccacccttg gcaagaatct tctcaactat tgggtattgat 240
gtcttcagct ggtatcatga attaccaagg atccataaag ctaccagctc ctgcggaagt 300
gaacctgaag ggcggaagg cactatttca caatatttta ctaccttaca ctgtcctgtg 360
tgtgatgacc taactcagca tggcatctgt agtaaagtgc ggagccaacc tcagcatgtt 420
gcagtcaccc tcaaccaaga aatccgggag ttggaacgtc aacaggagca acttgtaaag 480
atatgcaaga actgtacagg ttgctttgat cgacacatcc catgtgttct tctgaactgc 540
ccagtacttt tcaaaactctt ccgagtaaat agagaattgt ccaaggcacc atatcttcgg 600
cagttattaa accag                                     615

```

108

<210> 306
 <211> 504
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(504)
 <223> n = A,T,C or G

<400> 306
 gaattcggca cnaggccaaa acctgttttg gaagcatatt acagaaatga tttcaagtac 60
 cctgtattct ggatgctaaa aaacaaaaaac aaacaaaaaac acaaaaacaa aaaaacaaaa 120
 ccagaatcag gtaaaacagc tatgtgatta aaatatattta attcttcagc aattaccggy 180
 ttttctaaat tgaatcatgc atctatttat aattctaat attttgtaaa agaagacaaa 240
 attatgaatc ttaagtattt gctccatctt tttctctgta atgggtggaga ggctgcccac 300
 aattcatctc cacatggagc caagtttaat gtttctagtt cacattttgt acttctgtca 360
 tgcttatttc aaactccctg agtgatgggt aagaaatcaa acattgcctc agtggtatca 420
 agagaacttt ggtggtggtt tcttcagaat catgaagttc ttttgccaga taaatatttt 480
 gatattattt tcctttttta tata 504

<210> 307
 <211> 449
 <212> DNA
 <213> Homo sapiens

<400> 307
 gaattcggca cgagggtttta accctgctg gcaatccctg acgcaccgcc gtgatgccca 60
 gggaagacag ggcgacctgg aagtccaact acttccttaa gatcatccaa ctattggatg 120
 attatccgaa atgtttcatt gtgggagcag acaatgtggg ctccaagcag atgcagcaga 180
 tccgcatgtc ccttcgcggg aaggctgtgg tgctgatggg caagaacacc atgatgcgca 240
 aggccatccg agggcacctg gaaaacaacc cagctctgga gaaactgctg cctcatatcc 300
 gggggaatgt gggcctttgtg ttcaccaagg aggacctcac tgagatcagg gacatgttgc 360
 tggccaataa ggtgccagct gctgccgtgc tgggtgccatt gcccctatgt aagtcactgt 420
 gccagcccag aacactggtc tcggggccc 449

<210> 308
 <211> 524
 <212> DNA
 <213> Homo sapiens

<400> 308
 gaattcggca cgagggttga ttatggcaag aagtccaagc tggagttctc catttaccac 60
 gcaccccagg tttccacagc tgtagttgag ccctacaact ccctcctcac caccacacc 120
 accctggagc actctgattg tgcttcatg gtagacaatg aggccatcta tgacatctgt 180
 cgtagaaacc tcgatatcga gcgcccaccc tacactaacc ttaaccgcct tattagccag 240
 attgtgtcct ccatcactgc ttccctgaga tttgatggag ccctgaatgt tgacctgaca 300
 gaattccaga ccaacctggt gccctacccc cgcctccact tccctctggc cacatatgcc 360
 cctgtcatct ctgctgagaa agcctacccat gaacagcttt ctgtagcaga gatcaccaat 420
 gcttgctttg agccagccaa ccagatggtg aaatgtgacc ctgcgccatgg taaatacatg 480
 gcttgctgccc tgttgctaccg tggtagctg gttcccaaag atgt 524

<210> 309
 <211> 524
 <212> DNA
 <213> Homo sapiens

<400> 309
 gaattcggca cgagggttgc tcaactgagt cctactttta tgcctgacct gtggtgagca 60

109

caaatgttga	gcacatcaat	ccccattttg	tagacgaaga	gacagagttg	agtgactttg	120
ccaaagacac	agggccagtg	aggagtgtg	caggttttgc	ctggcattaa	aataataaac	180
attgaaattc	agtcgattcc	cctatggact	cagttataga	tctcatcagt	tgaagggaaga	240
gagatgcctt	ttcctattca	gcctttttgc	aatcctttcca	tctagaggag	atgtatctta	300
taatatactc	aaaggcactc	tggtgctaag	agcagccttg	atgaggtccc	atatagctca	360
ttggaagcag	agctagtctt	ggaaaactgaa	aatgttggac	cagagtctgc	ccatttcctt	420
agctctgggt	ccagctgtgg	tctgggttgg	aatggagtct	gaccttgcct	cacacagggc	480
ctgtctgttc	tcattgtggc	catccacatc	ctggagctgc	tcat		524

<210> 310

<211> 524

<212> DNA

<213> Homo sapiens

<400> 310

gaattcggca	cgaggggaga	ctacaaggat	aggcccagga	gtaatggagt	ccaaagagaa	60
acgagcagta	aacagtctca	gcatggaaaa	tgccaaccaa	gaaaatgaag	aaaaggagca	120
agttgctaag	aaaggggagc	ccttggccct	ccctttggat	gctggtgaat	actgtgtgcc	180
tagaggaagt	cgtaggcggt	tccgcgttag	gcagcccatc	ctgcagtata	gatgggatat	240
gatgcatagg	cttgaggaaac	cacaggcaag	gatgagagaa	gagaatatgg	aaaggattgg	300
ggaggaggtg	agacagctga	tggaaaagct	gagggaaaag	cagttgagtc	atagtctgcg	360
ggcagtcagc	actgaccccc	ctcaccatga	ccatcatgat	gagtttttgc	ttatgccctg	420
aatcctgatg	gtttccctaa	agttattacg	gaaacagacc	cctgctttcg	aattttacatg	480
ttcatgatgt	gcccttggtg	taaaccttta	cctgtcactt	gttt		524

<210> 311

<211> 523

<212> DNA

<213> Homo sapiens

<400> 311

gaattcggca	cgaggcctcg	tgccgtgccc	cccagggtat	gcgggggtcac	tcgctgctcg	60
atgttccctc	cgaagggctg	gacaaggctc	cggagccctg	tagctgccct	ccctaggagc	120
cccgggtctt	cactggccga	ggtgccacc	ccgcagcatt	ctgggagtgg	tagtttttctt	180
ccttcagggt	cattcctggc	tggccagtgc	ccaagactgg	cgagactacg	attcccagac	240
gccaagcga	gtcgccggtc	acgtggccgc	aaggacgctg	ggccggtggg	cgggggccgg	300
caggtgtctc	gcagccgtct	gtgccacca	gagccggcgg	gcccgtaggt	ccccggagac	360
cctgtctatg	tgcggtcggg	cgccgtgggg	gctcatctcc	ccgcgtccgg	cttgatatac	420
ttcggggacc	tgaagaagat	gaacaagcgc	cagctctatt	accaggtttt	aaacttcgcc	480
atgatcgtgt	cttctgcact	catgatattg	aaaggcttga	tcg		523

<210> 312

<211> 524

<212> DNA

<213> Homo sapiens

<400> 312

gaattcggca	cgagggtgaa	ggtgtgtgtc	agctttttgcg	tcactcgagc	cctgggcgct	60
gcttgctaaa	gagccgagca	cgcggtctg	tcatcatgtc	gcgttacggg	cggtacggag	120
gagaaaccaa	ggtgtatgtt	ggtaacctgg	gaactggcgc	tggcaaagga	gagttagaaa	180
gggctttcag	ttattatggt	cctttaagaa	ctgtatggat	tgcgagaaat	cctccaggat	240
ttgcctttgt	ggaattcgaa	gatcctagag	atgcagaaga	tgagtagcga	ggactggatg	300
gaaaggtgat	ttgtggctcc	cgagtggagg	ttgaactatc	gacaggcatg	cctcggagat	360
cacgttttga	tagaccacct	gcccagcgtc	cctttgatcc	aaatgataga	tgctatgagt	420
gtggcgaaaa	gggacattat	gcttatgatt	gtcatcgtaa	cagccggcga	agaagaagca	480
ggtcacggtc	tagatcacat	tctcgatcca	gaggaaggcg	atac		524

<210> 313

<211> 523

110

<212> DNA

<213> Homo sapiens

<400> 313

```

gaattcggca cgaggggtaa caccagaata tttggcaaag ggagaaaaaa aaagcagcga 60
ggcttcgcct tccccctctc cctttttttt tctctctctt ccttcctcct ccagccgccc 120
ccgaatcatg tcgatgagtc caaagcacac gactccgttc tcagtgtctg acatcttgag 180
tccccctggag gaaagctaca agaaagtggg catggagggc ggccggcctcg gggctccgct 240
ggcggcgctac aggcagggcc aggcggcacc gccaacagcg gccatgcagc agcacgccgt 300
ggggcaccac ggcgccgtca ccgccgccta ccacatgacg gcggcggggg tgccccagct 360
ctcgcactcc gccgtggggg gctactgcaa cggcaacctg ggcaacatga gcgagctgcc 420
gccgtaccag gacaccatga ggaacagcgc ctctggcccc ggatggtacg gcgccaaccc 480
agaccgcgcg ttccccgccg gttctttttt ttcaggatca ggc 523

```

<210> 314

<211> 525

<212> DNA

<213> Homo sapiens

<400> 314

```

gaattcggca cgaggggaaa ccagagatag agggaaagcc agagagtga gtagagccag 60
ggagtgaaac aagggctgca ggaaagcgcc cagctgagga tgatgtaccc aggaaagcca 120
aaagaaaaac taataagggg ctggctcatt acctcaagga gtataaagag gccatacatg 180
atatgaattt cagcaatgag gacatgataa gagaatttga caatatggct aaggtgcagg 240
atgagaagag aaaaagcaaa cagaaattgg gggcgttttt gtggatgcaa agaaatttac 300
aggaccctt ctaccctaga ggtccaaggg aattcagggg tggctgcagg gccccacgaa 360
gggacattga agacattcct tatgtgtagt gtccctggca ggcatttacc aggccatgtg 420
ctttaacgtt cggtataact ttactttagg catccctcct gttgctagca gccttttgac 480
ctatctgcaa tgcagtgttc tcagtaggaa atgttcatct gttac 525

```

<210> 315

<211> 358

<212> DNA

<213> Homo sapiens

<400> 315

```

gaattcggca cgaggggggtg gtggagcgct gggcgccag gctccctggc tggccgggtt 60
gggcgtctgg gccgtgaagg tgggacctcc tgttccgggc cgcaagtttc cctctccagc 120
cgccccgcgt tcgtagcatg tccccagaa ctccggggag gcaggcagga caggcttaga 180
gaagacgcgg tccccagcgc ttgggccacg gacgtccac cccgctcctc tgtcgttgga 240
gaaccgcggg gccgagccac tgggagaagc aggccagagc cttccagggc ctccggcccc 300
tggaccgcag gaggatgagc tggctttttc ccctgaccaa gagcgcctcc tctccgc 358

```

<210> 316

<211> 420

<212> DNA

<213> Homo sapiens

<400> 316

```

gaattcggca cgaggcgttc cttcgcacac tgtgattttg ccctcctgcc cagcagacc 60
tgcagcgggc aaagagctcc cgaggaagca cagcttgggt caggttcttg cctttcttaa 120
tttttagggac agctaccgga agggagggga caaggagtgc tcttccgcag cccctttccc 180
cacgcccacc cccagtctcc agggaccctt gcctgcctcc taggctggaa gccatggtcc 240
cgaagtgtag ggcaagggtg cctcaggacc ttttgggtct cagcctccct cagccccag 300
gatctgggtt aggtggccgt cctcctgctc ctcatgggaa gatgtctcag agccttcag 360
acctccctc cccaacccaa tgccaaagtg gacttgggag ctgcacaaag tcagcagga 420

```

<210> 317

<211> 518

111

<212> DNA

<213> Homo sapiens

<400> 317

```

gaattcggca cgagggctgc cggagggctgc ttttaaaggc cccgcgcgtt gccgccccct 60
cggcccgcca tgctgctatc cgtgccgctg ctgctcggcc tcctcggcct ggccgtcgcc 120
gagcctgccg tctacttcaa ggagcagttt ctggacggag acgggtggac ttcccgtgg 180
atcgaatcca aacacaagtc agattttggc aaattcgttc tcagttccgg caagttctac 240
ggtgacgagg agaaagataa aggtttgcag acaagccagg atgcaogctt ttatgctctg 300
tcggccagtt tcgagccttt cagcaacaaa ggccagacgc tgggtggtgca gttcacgggtg 360
aaacatgagc agaacatcga ctgtgggggc ggctatgtga agctgtttcc taatagtttg 420
gaccagacag acatgcacgg agactcagaa tacaacatca tgtttggtcc cgacatctgt 480
ggcctgcacc aaaaagggtc atgtcatctt caactaca                    518

```

<210> 318

<211> 401

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(401)

<223> n = A,T,C or G

<400> 318

```

aacaccaagg tggacaagag agttgagtcc aaatatggtc ccccatgccc atcatgcccc 60
gcacctgagt tcctgggggg accatcagtc ttcctgttcc ccccaaaacc caaggacact 120
ctcatgatct cccggacccc tgaggtcacg tgcgtggtgg tggacgtgag ccaggaagac 180
cccgaggtcc agttcaactg gtacgtggat ggcgtggagg tgcataatgc caagacaaaag 240
ccgcgggagg agcagttcaa cagcacgtac cgtgtggtca gcgtcctcac cgtcctgcac 300
caggactggc tgaacggcaa ggagtacaag tgcaaggctc ccaacaaagg cctcccgtcc 360
tccatcgaga aaacatntn caaagccaaa gggcagcccc g                    401

```

<210> 319

<211> 401

<212> DNA

<213> Homo sapiens

<400> 319

```

accgtgtact attagccatg gtcaacccca ccgtgttctt cgacattgcc gtcgacggcg 60
agcccttggg ccgcgtctcc tttgagctgt ttgcagacaa ggtcccaaag acagcagaaa 120
attttcgtgc tctgagcact ggagagaaag gatttggtta taagggttcc tgctttcaca 180
gaattattcc agggtttatg tgtcagggtg gtgacttcac acgccataat ggcactggtg 240
gcaagtccat ctatggggag aaatttgaag atgagaactt catcctaaag catacgggtc 300
ctgcatcttg tccatggcaa atgctggacc caacacaaat ggttcccagt ttttcatctg 360
cactgccaa g actgagtggg tggatggcaa gcatgtggtg t                    401

```

<210> 320

<211> 471

<212> DNA

<213> Homo sapiens

<400> 320

```

tagagtccca caaacccctt gcatgcctta atgtttgaga attocattct atttctcatt 60
aatctcttga aagcaaagat attttataaa tcttttttga ccagtgtttt agatggtagt 120
ggctgtggca gtgactttta attagccatc ctgaacccat catttaaaat atttattttt 180
gctttcagaa attttgaaat aagtaaggga aaaaacaaaa ttatttacag atacacataa 240
ccaacccaaa ataaaagcaa aatactaaat taggcacaca gaaagactaa aagtaaattc 300

```

112

```

actaggaaag acactcctca aagatagaat gtaaattttg tgaatccaga gtgctcaaac 360
cagaataacg cttgtcctta taccctaaag gacttgccaa gaaagataaa aagtatttta 420
ttatcccaga aagaatgcaa gggctctcat ttcagttggc ttataacacc a 471

```

<210> 321
 <211> 471
 <212> DNA
 <213> Homo sapiens

```

<400> 321
attactcaac agatttggac acaacggaaa gacaacagtt gatatttcta cttggtgtga 60
gcagtttgca actttttgtt cagagcaact ggacggggcc cctgttgac ttacaccctc 120
aggacttttt gtcattctgtt ttgttccagc aattcagtga ggttaaagga ctggatgcat 180
ttgttctgag cctgtcact ctagatgggtg aatcaatcta cagcctgacc tcgaagccta 240
tactactgtt attagcacgc attatcctag tgaatgtaag acataaactg acagctattc 300
agagcttgcc atgggtggact ttgagatgtg tgaatattca tcagcatttg cttgaggaac 360
gtcacctct gctttttact cttgccgaaa actgtattga tcaagtgatg aaactacaga 420
atctgtttgt agatgattca ggtcgatatt tggctattca attccatctg g 471

```

<210> 322
 <211> 601
 <212> DNA
 <213> Homo sapiens

```

<400> 322
tgaaggagca gttgccgcgc ttggcggcgc cccgagcagt tttcgctgct gctacggctg 60
ttgccatgag gcgaggctag ggaggacctc acttccccgg ggtgtaataa tgtaactga 120
ggccagtcta tccatatggg gatggggaag ccttggcatt gtcctttttc tgataacctt 180
tggaaccttt gtaatatattt atttgacatt ttatatcctc tgctttgttg gtgggggttt 240
agtggttact ctctgtttt gaaaaacaaa ctcagagaag tacctagaac agtgtgaaca 300
ctcatttctt cctccaacat cacctgggtt tcctaagtgc ttagaagaaa tgaaacggga 360
agccaggact attaagattg atagaagatt gacgggtgcc aatataattg atgaacctct 420
ccagcaagtt atccagtttt ccttgaggga ttatgtccag tatttggtatt atacactaag 480
cgatgatgaa tcttttcttc ttgaaattag gcagactctt caaaacgcac tcattcagtt 540
tgctactagg tcaaaagaaa tagactggca accttatttt actacacgca ttgtagatga 600
c 601

```

<210> 323
 <211> 601
 <212> DNA
 <213> Homo sapiens

```

<400> 323
gatgaggtag cagaggctca acgggcagag ttttagccctg cccagttctc tggtcctaag 60
aagatcaacc tgaaccactt gttgaatttc acttttgaac cccgtggcca gacgggtcac 120
tttgaaggca gtggacatgg tagctgggga aagaggaaca agtggggaca taagcctttt 180
aacaaggaac tctttttaca ggccaactgc caatttgttg tgtctgaaga ccaagactac 240
acagctcatt ttgctgatcc tgatacatta gttaactggg actttgtgga acaagtgcgc 300
at ttgtagcc atgaagtgcc atcttgccca atatgcctct atccacctac tgcagccaag 360
ataaccggtt gtggacacat cttctgctgg gcatgcatcc tgcactatct ttcactgagt 420
gagaagacgt ggagtaaatg tccatctgtg tacagtcttg tgcataagaa ggatctcaag 480
agtgttggtg ccacagagtc acatcagtat gttgttggtg ataccattac gatgcagctg 540
atgaagaagg agaaaggggt ggtggtggct ttgcccaaat ccaaattggat gaatgtagac 600
c 601

```

<210> 324
 <211> 461
 <212> DNA
 <213> Homo sapiens

113

<400> 324

```

catcttcttc ctttcgcggg gtcctccgta gttctggcac gagccaggcg tactgacagg 60
tggaaccagcg gactggtgga gatggcgacg ctctctctga ccgtgaattc aggagaccct 120
ccgctaggag ctttgctggc agtagaacac gtgaaagacg atgtcagcat ttccgttgaa 180
gaagggaaaag agaataattct tcatgtttct gaaaatgtga tattcacaga tgtgaattct 240
atacttcgct acttggttag agttgcaact acagctgggt tatatggctc taatctgatg 300
gaacatactg agattgatca cttggttgga gttcagtgtc acaaaattat cttcatgtga 360
ttcctttact tctacaatta atgaactcaa tcattgcctg tctctgagaa catacttagt 420
tggaactcc ttgagtttag cagatttatg tgtttgggcc a 461

```

<210> 325

<211> 461

<212> DNA

<213> Homo sapiens

<400> 325

```

tcacttttga accccgtggc cagacgggtc actttgaagg cagtggacat ggtagctggg 60
gaaagaggaa caagtgggga cataagcctt ttaacaagga actcttttta caggccaact 120
gccaatgtgt ggtgtctgaa gaccaagact acacagctca ttttgctgat cctgatacat 180
tagttaactg ggactttgtg gaacaagtgc gcattttagt ccatgaagtg ccatcttgcc 240
caatatgcct ctatccacct actgcagcca agataacccg ttgtggacac atcttctgct 300
gggcatgcat cctgcactat ctttactga gtgagaagac gtggagtaaa tgtcccatct 360
gttacagttc tgtgcataag aaggatctca agagtgttgt tgccacagag tcacatcagt 420
atgttggttg tgataccatt acgatgcagc tgatgaagaa g 461

```

<210> 326

<211> 451

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(451)

<223> n = A,T,C or G

<400> 326

```

ctgtggaggc cagttctgga gctattgcag cctcggttgc ccggccgggg acccgagccg 60
aaaagttatc gtcagaatgt cgggcaaaga ccgaattgaa atctttcoct cgcgaatggc 120
acagaccatc atgaangctc gtttaaaggg agcacagaca ggtcgaaacc tcctgaagaa 180
aaaatctgat gccttaactc ttcgatttcg acagatccta aagaagataa tagagactaa 240
aatgttgatg ggcgaagtga tgagagaagc tgccttttca ctagctgaag ccaagttcac 300
agcagggtgac ttcagcacta cagttatcca aaatgtcaat aaagcgcaag tgaagattcg 360
agcgaagaaa gataatgtag caggtgttac tttgccagta tttgaacatt accatgaagg 420
aactgacagt tatgaactga ctggtttagc c 451

```

<210> 327

<211> 601

<212> DNA

<213> Homo sapiens

<400> 327

```

gaggggaggc cagcgaagcc gagtaaaacc gccgcccggg agaagactga aggagcagtt 60
gccgcggttg gccgcggccc gagcagtttt cgctgctgct acggctgttg ccatgaggcg 120
aggctaggga ggacctcact tccccggggt gtaataatgt taactgaggc cagtctatcc 180
atatggggat ggggaagcct tggcattgtc ctttttctga taaccttttg accctttgta 240
atattttatt tgacatttta tatcctctgc tttgtgggtg ggggttttagt ggttactctc 300
ctgttttgaa aaacaaactc agagaagtac ctagaacagt gtgaacactc atttcttctc 360
ccaacatcac ctgggggttcc taagtgetta gaagaaatga aacgggaagc caggactatt 420

```

114

```

aagattgata gaagattgac ggggtgccaat ataattgatg aacctctcca gcaagttatc 480
cagtttttct tgaggggatta tgtccagtat tgggtattata cactaagcga tgatgaatct 540
tttcttcttg aaattaggca gactcttcaa aacgcactca ttcagtttgc tactaggtca 600
a                                                    601

```

```

<210> 328
<211> 601
<212> DNA
<213> Homo sapiens

```

```

<400> 328
ccggaatgat caccaagaca cacaaagtag accttgggct cccagagaag aaaaagaaga 60
agaaagtggg caaagaacca gagactcgat actcagtttt aaacaatgat gattactttg 120
ctgatgtttc tcctttaaga gctacatccc cctctaagag tgtggcccat gggcaggcac 180
ctgagatgcc tctagtgaag aaaaagaaga agaaaaagaa ggggtgtcagc accctttgcg 240
aggagcatgt agaacctgag accacgctgc ctgctagacg gacagagaag tcacccagcc 300
tcaggaagca ggtgtttggc cacttggagt tcctcagtg ggaaaagaaa aataagaagt 360
cacctctagc catgtcccat gcctctgggg tgaaaacctc cccagaccct agacagggtg 420
aggaggaaac cagagttggc aagaagctca aaaaacacaa gaaggaaaaa aagggggccc 480
aggacccac agccttctcg gtccaggacc cttggttctg tgaggccagg gagggcaggg 540
atgttgggga cacttgctca gtggggaaga aggatgagga acaggcagcc ttggggcaga 600
a                                                    601

```

```

<210> 329
<211> 501
<212> DNA
<213> Homo sapiens

```

```

<400> 329
agcagctttc gctccaagct gcattcttcta gacctcgctg gatcagaaag acagaagaaa 60
accaaggctg aaggggatcg tctaaaagag ggtattaata ttaaccgagg cctcctatgc 120
ttgggaaatg taatcagtcg tcttggagag gacaaaaagg gtggctttgt gccctacaga 180
gattccaagt tgactcgact gcttcaagat tctctaggag gtaatagcca tactcttatg 240
atagcctgtg tgagtccctg tgactccaat cttagaggaaa cattaaatac ccttcgctat 300
gctgacagag caagaaaaat caagaacaaa cctattgtta atattgatcc ccagacagct 360
gaacttaatc atctaaagca acaggtacaa cagctacaag tcttgttgct acaggcccat 420
ggaggtaccc tgccctggatc tataactgtg gaaccatcag agaactctaca atccctgatg 480
gagaagaatc agtccttggt a                                                    501

```

```

<210> 330
<211> 451
<212> DNA
<213> Homo sapiens

```

```

<400> 330
cgcgaggcgc gggccatgga acagcgggta gctgagtttc gggcgggcgc gaaacgggcg 60
ggtctggcgc cccaaccccc tgctgccagt cagggcgcac aaaccccgag agagaaggcg 120
gaagcagcag cgactctaaa ggcagcccca ggctggctaa agcggttcct ggtatggaaa 180
cctaggcccc cgagtgcctg ggcccagccc ggcctagttc aggaagcggc tcagccccag 240
ggcagcacat cacagacacc atggaacaca gccattcctc tgccgtcgtg ctggggaccag 300
tctttcctga ccaatatcac cttcttgaag gttcttctct ggttggtoct gctgggactg 360
tttgtggaac tgggaatttg cctgcatatt ttgtcctgtc cttgttctat tggatgtacg 420
tcgggacacg aggccttgaa gagaagaaag a                                                    451

```

```

<210> 331
<211> 331
<212> DNA
<213> Homo sapiens

```

115

<400> 331

```

cgttggtoct gtgcgggtcac ttagccaaga tgcctgagga aaccagacc caagaccaac 60
cgatggagga ggaggagggt gagacgttcg cctttcaggc agaaattgcc cagttgatgt 120
cattgatcat caatactttc tactcgaaca aagagatctt tctgagagag ctcatttcaa 180
attcatcaga tgcattggac aaaatcccgat atgaaagctt ggacagaatc caataaatta 240
aaacttcttg ggaaaagaag cttgcattat taacccttta taccgaacca aaccaaagaa 300
tccgaaactt cttcacttat ttggtgggga a 331

```

<210> 332

<211> 401

<212> DNA

<213> Homo sapiens

<400> 332

```

tccttcttga tcctgaactg ggtaggtgc cgctgttgc gctcgtgttg aatctagaac 60
cgtagccaga catgggactg gaggacgagc aaaagatgct taccgaatcc ggagatcctg 120
aggaggagga agaggaagag gaggaattag tggatccctt aacaacagtg agagagcaat 180
gcgagcagtt ggagaaatgt gtaaaggccc gggagcggct agagctctgt gatgagcgtg 240
tatctctctg atcacatata gaagaggatt gcacggagga gctctttgac ttcttgcattg 300
cgagggacca ttgctgtggc cacaaactct ttaacaactt gaaataaatg tgtggactta 360
attcacccca gtcttcatca tctgggcatc agaataatttc c 401

```

<210> 333

<211> 331

<212> DNA

<213> Homo sapiens

<400> 333

```

gatccctgca gaggcctcat ccccgacag cgagccagtc ctagagaagg atgacctcat 60
ggacatggat gcctctcagc agaatttatt tgacaacaag tttgatgaca tctttggcag 120
ttcattcagc agtgatccct tcaatttcaa cagtcaaaat ggtgtgaaca aggatgagaa 180
ggaccactta attgagcgac tatacagaga gatcagtgga ttgaaggcac agctagaaaa 240
catgaagact gagagccagc gggttgtgct gcagctgaag ggccacgtca gcgagctgga 300
agcagatctg gccgagcagc agcacctgcg g 331

```

<210> 334

<211> 551

<212> DNA

<213> Homo sapiens

<400> 334

```

agcgggactg gctgggtcgg ctgggctgct ggtgcgagga gccgcggggc tgtgctcggc 60
ggccaagggg acagcgcggt ggtggccgag gatgctgcgg gccggtagct ccggcgcccc 120
tagctggtga ctgctgcgcc gtgcctcaca cagccgaggc gggctcggcg cacagtcgct 180
gctccgcgcg cgcgcgccgg ggcgctccag gtgctgacag cgcgagagag cgcggccctc 240
aggagcaagg cgaatgtatg acaacatgtc cacaatggtg tacataaagg aagacaagtt 300
ggagaagctt acacaggatg aaattatttc taagacaaag caagtaattc aggggctgga 360
agctttgaag aatgagcaca attccatttt acaaagtgtg ctggagacac tgaagtgttt 420
gaagaaagat gatgaaagta atttggtgga ggagaaatca aacatgatcc cggaagtcac 480
tggagatggt taggctcggc ctgagtgagg cacaggttat gatggctttg tcaaatcacc 540
tgaatgcttg t 551

```

<210> 335

<211> 501

<212> DNA

<213> Homo sapiens

<400> 335

```

caggcgggccg agcgggactg gctgggtcgg ctgggctgct ggtgcgagga gccgcggggc 60

```

116

```

tgtgtctggc ggccaagggg acagcgcgtg ggtggccgag gatgctgogg ggcggtagct 120
ccggcgcccc tagctgggtga ctgctgcgcc gtgcctcaca cagccgaggc gggctcggcg 180
cacagtgcgt gctccgcgcg cgcgcccgcc ggcgctccag gtgctgacag cgcgagagag 240
cgcggccctc aggagcaagg cgaatgtatg acaacatgtc cacaatggtg tacataaagg 300
aagacaagtt ggagaagctt acacaggatg aaattatttc taagacaaag caagtaattc 360
aggggctgga agctttgaag aatgagcaca attccatttt acaaagtttg ctggagacac 420
tgaagtgttt gaagaaagat gatgaaagta atttggtgga ggagaaatca aacatgatcc 480
ggaagtcact ggagatgttg g 501

```

<210> 336

<211> 521

<212> DNA

<213> Homo sapiens

<400> 336

```

cctcggcgggc ggcgggcggtg cttacagcct gagaagagcg tctcgcccgg gagcgggcggc 60
ggccatcgag aoccacccaa ggcgcgctcc cctcggcctc ccagcgctcc caagccgcag 120
ogggcgcgcc ccttcagcta gctcgtcgcg tcgctctgct tccctgctgc cggctgcgcc 180
atggcggttg cgttggcgcc gctggcgccg gtcgagccgg cctgcggcag ccggtaccag 240
cagttgcaga atgaagaaga gtctggagaa cctgaacagg ctgcaggtga tgctcctcca 300
ccttacagca gcatttctgc agagagcgca gcataatttg actacaagga tgagtctggg 360
tttccaaagc ccccatctta caatgtagct acaacactgc ccagttatga tgaagcggag 420
aggaccaagg ctgaagctac tatcccttg gttcctggga gagatgagga ttttgtgggt 480
cgggatgatt ttgatgatgc tgaccagctg aggataggaa a 521

```

<210> 337

<211> 521

<212> DNA

<213> Homo sapiens

<400> 337

```

aaaggaggaa aatacacgga agagaattgc tgtcctggct gagtccagag agataactga 60
gggtcccaga caaggatcaa gagaacggga ttggcctcca gaggcagagg ttccaaatgg 120
gagtgggctt cctcctagaa agactttctg gaggagacct ccctactgtg taacagagga 180
ggactttggg attaagaaaa gcattccagg aagccgacag tgtcagcaaa cgtggagggtg 240
agatccttca aagtgagtggt tgtggagggt tccagaattt tctgagcctg aagggaaggt 300
tgagagcag accctgccct ttggaggctt gacttagccc tgagggcacc ctgtagccag 360
ggtgggcaga tgccaatatg gtagagacga agactgagta gggagccagc cacagtgtt 420
gtggtctcag gcaggggagt aagaccagag tggagcaggc tagaaacctg ggaaggaagc 480
aggttcccca gtataagccc atgatgtgtg aagaatgagc c 521

```

<210> 338

<211> 581

<212> DNA

<213> Homo sapiens

<400> 338

```

atactgcttg cttggagatg tcctcggaga ccattcttgc tatgacaagg cctgggagtt 60
gtcccggtag cgcagtgtc gtgctcagcg ctccaaagcc ctcccttcac ttccggaacaa 120
ggagtttcaa gagtgtgtag agtgcttcga acgctcgggt aagattaatc ccatgcagct 180
gggggtgttg ttttctctcg gttgtgccta tttggccttg gaagactatc aagggttcagc 240
aaaggcattt cagcgtctgt tgactctaga acccgataat gctgaagctt ggaacaattt 300
gtcaacttcc tatatccgat taaaacaaaa agtaaaagct tttagaactt tacaagaagc 360
tctcaagtgt aactatgaac actggcagat ttgggaaaac tacatcctca ccagcactga 420
cgttggggaa ttttcagaag ccattaaagc ttatcacccg ctcttggtgact tacgtgacaa 480
atacaaagat gttcaggctc ttaaaattct agtcagggca gtgattgatg ggatgactga 540
tcgaagtgga gatgttgcaa ctggcctcaa aggaagctg c 581

```

<210> 339

117

<211> 581

<212> DNA

<213> Homo sapiens

<400> 339

```

aagaagaaga agctcgcggt cgtgaagaag cagagagggt ccggcaggaa cgagagaagc 60
atttccagag agaagagcaa gagcgctgg agagaaagaa gcgacttgag gagattatga 120
aaagaaccag gagaacagaa gctacagata agaaaaccag tgatcagaga aacggtgata 180
tagccaaggg agctctcact ggaggaacag aggtgtctgc acttccatgt acaacaaacg 240
ctccgggaaa tggaaagcca gttggcagcc cacatgtggt tacctcacac cagtcaaaaag 300
aaaaaaaaaa gcgtgatgga atagctattg gatcaggtta caaaaaacaa tttttaaaaa 360
taagctaaca tctaagaaac atcattttgc ctatactgcc tccccaaaaa tcctgttttt 420
actcagtgaa cacctaagcc cactcagaaa tgttctggat tgtcattttc tccatccttt 480
agcaccttct tattttgggg ggagctctga agccttgcaa gaagtgggag agaaaaggac 540
caggtgtgac agaagggacg atttaagtta ttacaataaa c 581

```

<210> 340

<211> 571

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(571)

<223> n = A,T,C or G

<400> 340

```

ggtggcaaat tcaagtcctg ttaaccccg ggtgttcttt gatgtcagta ttggcgggtca 60
ggaagttggc cgcatagaaga tgcagctctt tgcagacggt gtgcctaaga cggccgagaa 120
cttttaggcag ttctgcaccg gagaattcag gaaagatggg gttccaatag gatacaaagg 180
aagcaccttc cacagggtca taaaggattt catgattcag ggtggagatt ttgttaatgg 240
agatggtact ggagtcgcca gtatttaccg ggggccattt gcagatgaaa attttaaaact 300
tagacactca gctccaggcc tgctttccat ggcgaacagt ggtccaagta caaatggctg 360
tcagttcttt atcaccctgct ctaagtgcga ttggctggat ggggaagcatg tgggtgtttgg 420
aaaaatcatc gatggacttc tagtgatgag aaagattgag aatgttccca caggcccca 480
caataagccc aagctacctg tggatgatct cagtgtgggg agatgtagtc cagacaaaaga 540
ctgaatcagt atacttgctc gacttcaagg n 571

```

<210> 341

<211> 581

<212> DNA

<213> Homo sapiens

<400> 341

```

taatgagacc aaagtttgca agggcaggac gagcccgtgc taacagagaa agtgttgttt 60
cctcaatttg gtttttagact gtcttgctct atgggggaga aaagatctgc ccttgggaga 120
ggtgccaact ttatagatct attaataaaa gaactggcag gcttacagtt cttgccaatg 180
aggaaacttg aatgagagaa gccaggctca accttggcca acagactgga gcccatcacc 240
ctaacttcac ccgcttctc cttacccaac cgtcaaaggc taggcagcac ccaccagca 300
gcttccacct ggctgaagcc tgcacctgct tcagaccaag ggttagatgg aaatttggca 360
tgggaagaga gggctcacct gtgggcagga tagactctat ccaagaagga gaactgaaaa 420
atgaaaacct atgagacaag gggatgatct gaagcaggca ggagaaaggg ctggaggagg 480
aggcactggg gaatttttcc tggatgaatac tgaagtact agatgttttg tcttgcaaaa 540
ctcaagggaa aactctcaaa ctctaattgt tggcctattc t 581

```

<210> 342

<211> 451

<212> DNA

<213> Homo sapiens

118

<400> 342

gcagaccaga	cttcgctcgt	actcgtgcgc	ctcgtctcgc	ttttcctccg	caaccatgtc	60
tgacaaaccc	gatatggctg	agatcgagaa	attcgataag	tcgaaactga	agaagacaga	120
gacgcaagag	aaaaatccac	tgctttccaa	agaaacgatt	gaacaggaga	agcaagcagg	180
cgaatcgtaa	tgaggcgtgc	gccgccaata	tgcaactgtac	attccacaag	cattgccttc	240
ttattttact	tcttttagct	gtttaacttt	gtaagatgca	aagaggttgg	atcaagttta	300
aatgactgtg	ctgccccctt	cacatcaaag	aactactgac	aacgaagccg	cgctgcctt	360
tcccatctgt	ctatctatct	ggctggcagg	gaaggaaaga	acttgcatg	ttggtgaagg	420
aagaagtggg	gggtggaaga	aatgggggtg	g			451

<210> 343

<211> 601

<212> DNA

<213> Homo sapiens

<400> 343

tgacctcatg	gacatggatg	cctctcagca	gaattttattt	gacaacaagt	ttgatgacat	60
ctttggcagt	tcattcagca	gtgatccctt	caattttcaac	agtcaaaatg	gtgtgaacaa	120
ggatgagaag	gaccacttaa	ttgagcgact	atacagagag	atcagtggat	tgaaggcaca	180
gctagaaaac	atgaagactg	agagccagcg	ggttgtgctg	cagctgaagg	gccacgtcag	240
cgagctggaa	gcagatctgg	ccgagcagca	gcacctgcgg	cagcaggcgg	ccgacgactg	300
tgaattcctg	cgggcagaac	tgagcgagct	caggaggcag	cgaggaggaca	ccgagaaggc	360
tcagcggagc	ctgtctgaga	tagaaaaggaa	agctcaagcc	aatgaacagc	gatatagcaa	420
gctaaaggag	aagtacagcg	agctggttca	gaaccacgct	gacctgctgc	ggaagaatgc	480
agaggtgacc	aaacaggtgt	ccatggccag	acaagcccag	gtagatttgg	aacgagagaa	540
aaaagagctg	gagggattcg	ttggagccgc	tcagtgaacc	agggccagcg	ggaagactca	600
a						601

<210> 344

<211> 571

<212> DNA

<213> Homo sapiens

<400> 344

gcgacccggg	gagcgagcac	gtcgtccgc	accgctcttc	ctccagccgc	tgagccgtcc	60
cttctcgcca	tgtcccagag	caggcaccgc	gccgaggccc	cgccgctgga	gcgagaggac	120
agtgggacct	tcagtttggg	gaagatgata	acagctaagc	cagggaaaac	accgattcag	180
gtattacacg	aatacggcat	gaagaccaag	aacatcccag	tttatgaatg	tgaagatct	240
gatgtgcaaa	tacacgtgcc	cactttcacc	ttcagagtaa	ccgttgggtga	cataacctgc	300
acaggtgaag	gtacaagtaa	gaagctggcg	aaacatagag	ctgcagaggc	tgccataaac	360
atthttgaaag	ccaatgcaag	tatttgcttt	gcagttcctg	accccttaat	gcctgaccct	420
tccaagcaac	caaagaacca	gcttaatcct	attggttcat	tacaggaatt	ggctattcat	480
catggctgga	gacttctga	atataccctt	tcccaggaag	gaggacctgc	tcataagaga	540
gaatatacta	caatttgtag	gctagagtca	t			571

<210> 345

<211> 551

<212> DNA

<213> Homo sapiens

<400> 345

gacctggcgc	tttgtgcggc	tccaggcctc	cgagtggact	ccagaaagcc	tgaaaagcta	60
tcatggcagc	aaggcccaag	ctccactatc	ccaacggaag	aggccggatg	gagtccgtga	120
gatgggtttt	agctgccgcc	ggagtgcagt	ttgatgaaga	atthctggaa	acaaaagaac	180
agttgtacaa	ggtgcaggat	ggtaaccacc	tgctgttoca	acaagtggcc	atggttgaaa	240
ttgacgggat	gaagtggta	cagacccgaa	gcattctoca	ctacatagca	gacaagcaca	300
atctcttttg	caagaacctc	aaggagagaa	ccctgtactg	tgccccctct	cgagtgttgt	360
cacttgtcag	cttactgatg	ccttagctga	ttagcaacct	ctgtagcaca	ccacatttac	420

119

```

tttatgtctt acatagttag tgagatcagg gaacaaaaaac ccaagaagggt cacgaagacc 480
agttggaact tcagtagaga gagtctgagt aaaacaaaaag aatagggtatt cagatattga 540
atactatatc t 551

```

```

<210> 346
<211> 501
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

```

```

<400> 346
tatgggaaac tgctctttat ttagaccttt gggacaaaat taacttttgggt cacatattac 60
ttaaaaaaaaa atccagtttt acatatttct aaatagatag aactaaatga tcagagaatt 120
tcttctgtaa aaattggcca aattttatca aaaatctaac atacgataca atccaaatta 180
taaaaagact acttgggatc ataattattcc aaatgtatga cagttataac tccatcttaa 240
caagngtgaa aagtacttgc tctcatgttg ctttgggtcca aaagagtaga gctaactcag 300
taacaggcaa ctaagtaccc aatcttttgc caaaattaat ttanattgtg actggcagca 360
gaaatatcca taatgaacag ctctactata acaaagaata attaaagaat acttttcgtg 420
aacatatcac agtatcaaat acattttttat aagagaaaaa tatgaaggaa atgataaaat 480
agctatcaca aacaaaaaga a 501

```

```

<210> 347
<211> 621
<212> DNA
<213> Homo sapiens

```

```

<400> 347
gcccggggaga agactgaagg agcagttgcc gccgttggcg gcggcccgag cagttttcgc 60
tgctgctacg gctgttgcca tgaggcgagg ctagggagga cctcacttcc ccgggggtgta 120
ataatgttaa ctgaggccag tctatccata tggggatggg gaagccttgg cattgtcctt 180
tttctgataa cctttggacc ctttgaata ttttatttga cattttatat cctctgcttt 240
gtgggtgggg gtttagtggt tactctcctg tttggaaaaa caaactcaga gaagtacctt 300
gaacagtgtg aacactcatt tcttcctcca acatcacctg gggttcctaa gtgcttagaa 360
gaaatgaaac ggggaagccag gactattaag attgatagaa gattgacggg tgccaatata 420
attgatgaac ctctccagca agttatccag ttttccttga gggattatgt ccagtattgg 480
tattatacac taagcgatga tgaatctttt cttcttgaaa ttaggcagac tcttcaaaac 540
gcactcattc agtttgctac taggtcaaaa gaaatagact ggcaacctta ttttactacc 600
cgcattgtag atgactttgg c 621

```

```

<210> 348
<211> 511
<212> DNA
<213> Homo sapiens

```

```

<400> 348
cggcgggcgg cgggcggcga tggcgggcgg ggaggccggt ggcgacgacg cccgctgcgt 60
cgggctgagc gccgagcggg cacaggcgct gctggccgac gtggacacgc tgctgttcga 120
ctgogacggc gtgctgtggc gcggggagac gcgcgtgcct ggcgcgcccg aggcctgcg 180
ggcgctgcga gcccgcgga agcgccctgg cttcatcacc aacaacagca gcaagaccg 240
cgctgcctac gccgagaagc tgcggcgccct gggcttcggc ggccccgcgg ggccccgcgc 300
cagcctggag gtcttcggca cggcctactg caccgcgctc tacctgcgcc agcgccctggc 360
cggcgccccc gcgcccaagg cctacgtgct gggcagccca gccctggcgg cggagctgga 420
gccgtgggag tcgccagcgt gggcggtggg cccgaccact gcagggcgag ggtcccggcg 480
actggctgca cgcccgcttg agccgactgc g 511

```

120

<210> 349
 <211> 521
 <212> DNA
 <213> Homo sapiens

<400> 349
 gctcaggcgc ctgaggctgg gtgagcgac gcgaggcggc gaggcggcag cgtgtttcta 60
 ggtcgtggcg tgggcttcc ggagctttgg cggcagctag gggaggatgg cggagtcttc 120
 ggataagctc tatcgagtcg agtacgcaa gagcgggcgc gcctcttgca agaaatgcag 180
 cgagagcatc cccaaggact cgctccggat ggccatcatg gtgcagtcgc ccatgtttga 240
 tggaaaagtc ccacactggt accactttctc ctgcttctgg aaggtgggccc actccatccg 300
 gcacctgac gttgaggtgg atgggttctc tgagcttcgg tgggatgacc agcagaaagt 360
 caagaagaca gcggaagctg gaggagtgc aggcaaaggc caggatggaa ttggtagcaa 420
 ggcagagaag actctgggtg actttgcagc agagtatgcc aagtccaaca gaagtacgtg 480
 caaggggggtg tatggagaag aatagaaaaa gggccaggtg c 521

<210> 350
 <211> 451
 <212> DNA
 <213> Homo sapiens

<400> 350
 gccggcgggc ggcgatggcg gcggcggagg ccggtggcga cgacgccgc tgcgtgcggc 60
 tgagcgccga gcgggcacag gcgctgctgg ccgacgtgga cacgctgctg ttgactgcg 120
 acggcgtgct gtggcgcggg gagaccgccg tgcctggcgc gcccgaggcc ctgcgggcgc 180
 tgcgagcccg cggcaagcgc ctgggcttca tcaccaacaa cagcagcaag acccgcgctg 240
 cctacgcoga gaagctgcgg cgctgggctc tcggcgggccc cgcggggccc ggcgccagcc 300
 tggaggtctt cggcacggcc tactgcaccg cgctctacct gcgccagcgc ctggccggcg 360
 cccccgcgcc caaggcctac gtgctgggca gccagccct ggccgcggag ctggagccgt 420
 gggcgtcgcc agcgtgggcg tggggcccga c 451

<210> 351
 <211> 581
 <212> DNA
 <213> Homo sapiens

<400> 351
 agagagagag agagagagag agagagagag agagagacct cgtgccgaat tcggcacgag 60
 gcctcgtgcc ggaaacttag tgatggacaa gttggtggtt tcataaatta tcgagatagc 120
 aagttaacac gaattctcca gaattccttg ggaggaaatg caaagacacg tattatctgc 180
 acaattactc cagtatcttt tgatgaaaca cttactgctc tccagtttgc cagtactgct 240
 aaatatatga agaatactcc ttatgttaat gaggtatcaa ctgatgaagc tctcctgaaa 300
 aggtatagaa aagaaataat ggatcttaaa aaacaattag aggaggtttc tttagagacg 360
 cgggctcagg caatggaaaa agaccaattg gccactttt ggaagaaaaa gatttgcttc 420
 agaaagtaca gaatgagaaa attgaaaact taacacggat gctggtgacc tcttcttccc 480
 tcacgttgca ccaggaatta aaggctaaaa gaaaacgaag agttacttgg tgccttgcaa 540
 aattaccaa tgaagaactc aacttttcag atcattttat t 581

<210> 352
 <211> 461
 <212> DNA
 <213> Homo sapiens

<400> 352
 aaaggcgatg aggtggatgg agtggatgaa gtggcgaaaga agaaatctaa aaaagaaaaa 60
 gacaaggata gtaagcttga aaaagcccta aatgacctga acgacctgat ctggaacatc 120
 aaggacgagc taaagaaagt gtgttcaact aatgacctga aggagctact catcttcaac 180
 aagcagcaag tgccttctgg ggagtcggcg atcttggacc gagtagctga tggcatggtg 240
 ttcggtgccc tccttccctg cgaggaatgc tcgggtcagc tggctcttcaa gagcgatgcc 300

121

```
tattactgca ctggggacgt cactgcctgg accaagtgt tggccaagac acagacaccc 360
aaccggaagg agtgggtaac cccaaaggaa ttccgagaaa tctcttacct caagaaattg 420
aaggttaaaa agcaggaccg tatattcccc ccagaaccag c 461
```

```
<210> 353
<211> 491
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(491)
<223> n = A,T,C or G
```

```
<400> 353
atggcggcgg cggaggccgg tggcgacgac gcccgtgctg tggcgctgag cgccgagcgg 60
gcacaggcgc tgctggccga cgtggacacg ctgctgttcg actgcgacgg cgtgctgtgg 120
cgcggggaga cgcgcgtgcc tggcgcgccc gaggcctgc gggcgctgag agcccgcggc 180
aagcgcctgg gcttcacac caacaacagc agcaagaccc gcgctgccta cgccgagaag 240
ctgcggcgcc tgggcttcgg cggccccgcg gggccccggc ccagcctgga ggtcttcggc 300
acggcctact gcaccgcgct ctacctgcgc cagcgcctgg ccggcgcccc cgcgcccaag 360
gcctacgtgc tgggcaaccc agccctggcc gcgganctgg agccgtgggc gtcgccagcg 420
tgggcgctgg gcccgaccac tgcaagggca gggccccggc gactggctga cgccccgctg 480
gaacccgact g 491
```

```
<210> 354
<211> 401
<212> DNA
<213> Homo sapiens
```

```
<400> 354
ggcgctcccg tgtggctgtg ccgttggtcc tgtgcggtca cttagccaag atgcctgagg 60
aaacccagac ccaagaccaa ccgatggagg aggaggagggt tgagacgttc gcctttcagg 120
cagaaattgc ccagttgatg tcattgatca tcaatacttt ctactcgaac aaagagatct 180
ttctgagaga gctcatttca aattcatcag atgcattgga caaaatccgg tatgaaagct 240
tgacagatcc cagtaaatta gactctggga aagagctgca tattaacctt ataccgaaca 300
aacaagatcg aactctcact attgtggata ctggaattgg aatgaccaag gctgacttga 360
tcaataacct tgggtactat gccaaagtct ggaccaaaagc g 401
```

```
<210> 355
<211> 451
<212> DNA
<213> Homo sapiens
```

```
<400> 355
tcttcagcgc atcagaagta tccagaatgt tcttgaaagc tcaggggctg tggaaactgt 60
tccagcattt caagaaatta cttctatgaa agaacgatgc aacaagcttc ttcagaaagt 120
tcagaaaaat aaagaattgg tgcagactga aatccaagaa agacattcct tcacaaaaga 180
gataattgct ttgaagaatt tctttcaaca gaccacaact tcattccaaa atatggcatt 240
ccaggatcac ccagaaaagt cagaacaatt tgaggagctt caaagcatcc ttaagaaagg 300
gaaactaact ttgagaata ttatggaaaa actgcgaatc aagtattccg aaatgtacac 360
catagtccct gcagagattg aatcccagggt ggaagaatgc agaaaagctt tagaagacat 420
agatgagaag attagccaat gaagtcttaa a 451
```

```
<210> 356
<211> 441
<212> DNA
<213> Homo sapiens
```

122

<220>
 <221> misc_feature
 <222> (1)...(441)
 <223> n = A,T,C or G

<400> 356
 gtcgcgcatc cggcgggcca tgaacgcctt catggtgtgg gcaaaggacg agcgcaagcg 60
 gctggctcag cagaacccgg acctgcacaa cgcggtgctc agcaagatgc tgggcaaagc 120
 gtggaaggag ctgaacgcgg cggagaagcg gcccttcgtg gaggaagccg aacggctgcg 180
 cgtgcagcac ttgcgcgacc accccaacta caagtaccgg ccgcgccgca agaagcaggc 240
 gcgcaaggcc cggcggctgg agcccggctc tgctcccggg attagcggcc ccgcagccac 300
 cgccgacctt tcccgcggcg tctggctcgn tcgcgccttc cgcgagctgc cccgctgggc 360
 gccgagttca cggctggggc tgccaccccg agcgtcgctc tgacggctga cccgggagct 420
 gcttttccac gccgcgcgcc a 441

<210> 357
 <211> 451
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(451)
 <223> n = A,T,C or G

<400> 357
 gcggcggcgg aggccgggtg cgacgacgcc cgctgcgtgc ggctgagcgc cgagcgggca 60
 caggcgctgc tggccgacgt ggacacgctg ctgttogact ggcacggcgt gctgtggcgc 120
 ggggagaccg ccgtgcctgg cgcgcccgag gccctgcggg cgctgcgagc ccgcggcaag 180
 cgctgggct tcatcaccaa caacagcagc aagaccgcgg ctgcctacgc cgagaagctg 240
 cggcgctgg gcttcggcgg ccccgcgggg cccggcgcca gectggaggt cttcggcacg 300
 gcctactgca ccgcgctcta cctgcgccag cgcctggcgg gcgccccgc gcccaagcct 360
 acgtgctggg cagcccagcc ctggccgcgg anctggaagc cgtgggcgtc gccagcgtgg 420
 gcgtggggcc cgaaccactt gcagggcgag g 451

<210> 358
 <211> 571
 <212> DNA
 <213> Homo sapiens

<400> 358
 gcggcgatgg cggcggcgga ggccggtggc gacgacgccc gctgcgtgcg gctgagcgcc 60
 gagcgggcac aggcgctgct ggccgacgtg gacacgctgc tgttcgactg cgacggcgtg 120
 ctgtggcgcg gggagaccgc cgtgcctggc ggcgccgagg ccctgcgggc gctgcgagcc 180
 cgcggcaagc gcctgggctt catcaccaac aacagcagca agaccgcgc tgccctacgc 240
 gagaagctgc ggcgctggg cttcggcggc cccgcggggc ccggcgccag cctggaggtc 300
 ttcggcacag cctactgcac cgcgctctac ctgcgccagc gcctggccgg cgccccgcg 360
 cccaagccta cgtgctgggc agcccagccc tggccgcgga gctggaggcc gtgggcgtcg 420
 ccagcgtggg cgtggggccc gaccactgca gggcgagggg cccggcgact ggctgcacgc 480
 gccgctggag cccgacgtgc gcgcggtggg ggtgggcttt gaccgcgact tagctacatg 540
 aagctcacca agcccttgcg ctacttgaag a 571

<210> 359
 <211> 511
 <212> DNA
 <213> Homo sapiens

<400> 359
 cgctgctgtt atggccgcct ccttgaggta gtatccgcac atggaattct agggccgcag 60

123

```

gtgtattttac ggtaactgtc gccactagat ttcagcgcct ttggactctc ctgttttcac 120
tttcttttgt tgactcccgt gtggccctcg tgggagcctg ttttggtgc agcgggtgtct 180
ggggtgatgt ggaccccgga gctggcaatt ctgaggggat tccccactga ggctgagcgg 240
cagcaatgga aacaggaggg ggctcgtcgt tcagagagt gatctttcct acaattgctg 300
ctggaaggga actatgaagc catattctta aattcaatga ctcaaaatat ttttaattca 360
acaacaaccg ctgaagaaaa gattgatagc tacctggaga agcaggtagt aacattcctg 420
gattactcaa cagatttgga cacaacgga agacaacagt tgatatttct acttggtgtg 480
agcagtttgc aactttttgt tcaaagcaac t 511

```

<210> 360

<211> 481

<212> DNA

<213> Homo sapiens

<400> 360

```

gcgttctcgg ggagctgctg ccgtagctgc cgccgcgcgt accaccgcgt tcgggtgtag 60
aatttggaat ccctgcgcgg cgtaacaat gaagcagagt tcgaacgtgc cggctttcct 120
cagcaagctg tggacgcttg tggaggaaac ccacactaac gagttcatca cctggagcca 180
gaatggccaa agttttctgg tcttgatga gcaacgattt gcaaaagaaa ttcttcccaa 240
atatttcaag cacaataata tggcaagctt tgtgaggcaa ctgaatatgt atgggttccg 300
taaagtagta catatcgact ctggaattgt aaagcaagaa agagatggtc ctgtagaatt 360
tcagcatcct tacttcaaac aaggacagga tgacttgttg gagaacatta aaaggaaggt 420
ttcatcttca aaaccagaag aaaataaaat tcgtcaggaa gatttaacaa aaattataag 480
t 481

```

<210> 361

<211> 551

<212> DNA

<213> Homo sapiens

<400> 361

```

cgtagaggaa gacactgtgg aggccagttc tggagctatt gcagcctcgg ttgcccggcc 60
ggggacccga gccgaaaagt tatcgtcaga atgtcgggca aagaccgaat tgaaatcttt 120
ccctcgcgaa tggcacagac catcatgaag gctcgtttaa agggagcaca gacaggctga 180
aacctcctga agaaaaaatc tgatgcctta actcttcgat ttcgacagat cctaaagaag 240
ataatagaga ctaaaatggt gatgggcgaa gtgatgagag aagctgcctt ttcactagct 300
gaagccaagt tcacagcagg tgacttcagc actacagtta tccaaaatgt caataaagcg 360
caagtgaaga ttcgagcgaa gaaagataat gtagcaggtg ttactttgcc agtatttgaa 420
cattaccatg gaaggagagg cagttatgaa ctgactgggt tagccagagg tggggaacag 480
ttggctaaat taaagaggaa ttatgcccaa agcagtggaa ctactggtgg aactagcttc 540
tcttcagac t 551

```

<210> 362

<211> 481

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(481)

<223> n = A,T,C or G

<400> 362

```

gggttacatt ttggattaaa cctgtttccc gggtatgtgt agggaaacagc aaagngatgc 60
acnaactttg aacattcgtt atggggaaaa catcctttta cttcgggggtc gtctgccaaa 120
gcagggtctg ggagggtcca tgcagttccc gntggtgtgg agggaaatgc cctggtctgg 180
cctccgagcc cccaggtcca ccgtctcccc tcccctcatt tgtaanaata gctacacact 240
aacatttttg gaaggagagg cacataaact tttttaacat ttggtaacta ggttatgggc 300
tctacattgt cagctacttg ggatatatat ttaattttct taaattcccg ttaactcta 360

```

124

ttttatggtt ttgatttcag attgcaaaca tgtaaaacct gcatagcago gagttctcgg 420
 ttttgcggtt tcttttagttc tttactgtca ctgtcatgta atcagctaata tctcttctgg 480
 a 481

<210> 363

<211> 461

<212> DNA

<213> Homo sapiens

<400> 363

ggaaccagga cctcggcgtg gcctagcgag ttatggcgac gaaggccgtg tgcgtgctga 60
 agggcgacgg cccagtgacg ggcacatcatc atttcgagca gaaggaaagt aatggaccag 120
 tgaaggtgtg gggaagcatt aaaggactga ctgaaggcct gcatggattc catgttcattg 180
 agtttgagga taatacagca ggctgtacca gtgcaggctc tcactttaat cctctatcca 240
 gaaaacacgg tgggccaaag gatgaagaga ggcattgttg agacttgggc aatgtgactg 300
 ctgacaaaga tgggtgtggc gatgtgtcta ttgaagattc tgtgatctca ctctcaggag 360
 accattgcat cattggccgc acactgggtg tccatgaaaa acagatgact tgggcaaagg 420
 tggaaatgaa gaaagtacaa agacaggaaa cgcttgaaagt c 461

<210> 364

<211> 531

<212> DNA

<213> Homo sapiens

<400> 364

ggttctactt tctgcacgtc agaaatcaat tccatgtcag ctcgagtcct gctcttgctg 60
 gtggtccag gccatctgat tttctctac atcatctacc tgggtggagg tcagtcagtc 120
 ataaacagcc agacctttgt ggtgctctac ctgctggcag gcctgatcca ggtgacaatc 180
 ctgctgtacc tcgcagaagt gatggttcgg ctgacttggc accaggccct ggatcctgac 240
 aaccactgca tcccctacct tacagggctg ggggacctgc tcggtagctg cctcctggca 300
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<210> 365

<211> 4834

<212> DNA

<213> Homo sapiens

<400> 365

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126

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agctgaatct ttttggtaac tttaaattct tatcatagac tctgtacata tgttcaaatt 4620
agctgcttgc ctgatgtgtg tatcatcggt gggatgacag aacaaacata tttatgatca 4680
tgaataatgt gctttgtaaa aagatttcaa gttattagga agcatactct gttttttaat 4740
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<210> 366

<211> 818

<212> PRT

<213> Homo sapiens

<400> 366

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Met Glu His Gly Gly Ala Thr Phe Ile Asn Ala Phe Val Thr Thr Pro
      20      25      30
Met Cys Cys Pro Ser Arg Ser Ser Met Leu Thr Gly Lys Tyr Val His
      35      40      45
Asn His Asn Val Tyr Thr Asn Asn Glu Asn Cys Ser Ser Pro Ser Trp
      50      55      60
Gln Ala Met His Glu Pro Arg Thr Phe Ala Val Tyr Leu Asn Asn Thr
      65      70      75      80
Gly Tyr Arg Thr Ala Phe Phe Gly Lys Tyr Leu Asn Glu Tyr Asn Gly
      85      90      95
Ser Tyr Ile Pro Pro Gly Trp Arg Glu Trp Leu Gly Leu Ile Lys Asn
      100      105      110
Ser Arg Phe Tyr Asn Tyr Thr Val Cys Arg Asn Gly Ile Lys Glu Lys
      115      120      125
His Gly Phe Asp Tyr Ala Lys Asp Tyr Phe Thr Asp Leu Ile Thr Asn
      130      135      140
Glu Ser Ile Asn Tyr Phe Lys Met Ser Lys Arg Met Tyr Pro His Arg
      145      150      155      160
Pro Val Met Met Val Ile Ser His Ala Ala Pro His Gly Pro Glu Asp
      165      170      175
Ser Ala Pro Gln Phe Ser Lys Leu Tyr Pro Asn Ala Ser Gln His Ile
      180      185      190
Thr Pro Ser Tyr Asn Tyr Ala Pro Asn Met Asp Lys His Trp Ile Met
      195      200      205
Gln Tyr Thr Gly Pro Met Leu Pro Ile His Met Glu Phe Thr Asn Ile
      210      215      220
Leu Gln Arg Lys Arg Leu Gln Thr Leu Met Ser Val Asp Asp Ser Val
      225      230      235      240
Glu Arg Leu Tyr Asn Met Leu Val Glu Thr Gly Glu Leu Glu Asn Thr
      245      250      255
Tyr Ile Ile Tyr Thr Ala Asp His Gly Tyr His Ile Gly Gln Phe Gly
      260      265      270
Leu Val Lys Gly Lys Ser Met Pro Tyr Asp Phe Asp Ile Arg Val Pro
      275      280      285
Phe Phe Ile Arg Gly Pro Ser Val Glu Pro Gly Ser Ile Val Pro Gln
      290      295      300
Ile Val Leu Asn Ile Asp Leu Ala Pro Thr Ile Leu Asp Ile Ala Gly
      305      310      315      320
Leu Asp Thr Pro Pro Asp Val Asp Gly Lys Ser Val Leu Lys Leu Leu
      325      330      335
Asp Pro Glu Lys Pro Gly Asn Arg Phe Arg Thr Asn Lys Lys Ala Lys
      340      345      350
Ile Trp Arg Asp Thr Phe Leu Val Glu Arg Gly Lys Phe Leu Arg Lys
      355      360      365
Lys Glu Glu Ser Ser Lys Asn Ile Gln Gln Ser Asn His Leu Pro Lys

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127

370		375		380
Tyr Glu Arg Val Lys Glu Leu Cys Gln Gln Ala Arg Tyr Gln Thr Ala				
385		390		395
Cys Glu Gln Pro Gly Gln Lys Trp Gln Cys Ile Glu Asp Thr Ser Gly				400
	405		410	
Lys Leu Arg Ile His Lys Cys Lys Gly Pro Ser Asp Leu Leu Thr Val				415
	420		425	
Arg Gln Ser Thr Arg Asn Leu Tyr Ala Arg Gly Phe His Asp Lys Asp				430
	435		440	
Lys Glu Cys Ser Cys Arg Glu Ser Gly Tyr Arg Ala Ser Arg Ser Gln				445
	450		455	
Arg Lys Ser Gln Arg Gln Phe Leu Arg Asn Gln Gly Thr Pro Lys Tyr				460
465		470		475
Lys Pro Arg Phe Val His Thr Arg Gln Thr Arg Ser Leu Ser Val Glu				480
	485		490	
Phe Glu Gly Glu Ile Tyr Asp Ile Asn Leu Glu Glu Glu Glu Glu Leu				495
	500		505	
Gln Val Leu Gln Pro Arg Asn Ile Ala Lys Arg His Asp Glu Gly His				510
	515		520	
Lys Gly Pro Arg Asp Leu Gln Ala Ser Ser Gly Gly Asn Arg Gly Arg				525
	530		535	
Met Leu Ala Asp Ser Ser Asn Ala Val Gly Pro Pro Thr Thr Val Arg				540
545		550		555
Val Thr His Lys Cys Phe Ile Leu Pro Asn Asp Ser Ile His Cys Glu				560
	565		570	
Arg Glu Leu Tyr Gln Ser Ala Arg Ala Trp Lys Asp His Lys Ala Tyr				575
	580		585	
Ile Asp Lys Glu Ile Glu Ala Leu Gln Asp Lys Ile Lys Asn Leu Arg				590
	595		600	
Glu Val Arg Gly His Leu Lys Arg Arg Lys Pro Glu Glu Cys Ser Cys				605
	610		615	
Ser Lys Gln Ser Tyr Tyr Asn Lys Glu Lys Gly Val Lys Lys Gln Glu				620
625		630		635
Lys Leu Lys Ser His Leu His Pro Phe Lys Glu Ala Ala Gln Glu Val				640
	645		650	
Asp Ser Lys Leu Gln Leu Phe Lys Glu Asn Asn Arg Arg Arg Lys Lys				655
	660		665	
Glu Arg Lys Glu Lys Arg Arg Gln Arg Lys Gly Glu Glu Cys Ser Leu				670
	675		680	
Pro Gly Leu Thr Cys Phe Thr His Asp Asn Asn His Trp Gln Thr Ala				685
	690		695	
Pro Phe Trp Asn Leu Gly Ser Phe Cys Ala Cys Thr Ser Ser Asn Asn				700
705		710		715
Asn Thr Tyr Trp Cys Leu Arg Thr Val Asn Glu Thr His Asn Phe Leu				720
	725		730	
Phe Cys Glu Phe Ala Thr Gly Phe Leu Glu Tyr Phe Asp Met Asn Thr				735
	740		745	
Asp Pro Tyr Gln Leu Thr Asn Thr Val His Thr Val Glu Arg Gly Ile				750
	755		760	
Leu Asn Gln Leu His Val Gln Leu Met Glu Leu Arg Ser Cys Gln Gly				765
	770		775	
Tyr Lys Gln Cys Asn Pro Arg Pro Lys Asn Leu Asp Val Gly Asn Lys				780
785		790		795
Asp Gly Gly Ser Tyr Asp Leu His Arg Gly Gln Leu Trp Asp Gly Trp				800
	805		810	
Glu Gly				815

<210> 367

128

<211> 361
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(361)
 <223> n = A,T,C or G

<400> 367
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 gctggcggct tccaacanat aaacttttgg acaaaggnac aanatatttt tgggcattca 180
 ttttaataac catctagtta tccaattagg aggnctctaa aaaaataaat atgacaaata 240
 tatggatttc tgaagtataa actgacatac aaatctatat attttcttaa tacttttcat 300
 taaagcatct ttaaagcatt ctgtaacatg aagttganag ttcaaattan atgtaatgaa 360
 a 361

<210> 368
 <211> 558
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(558)
 <223> n = A,T,C or G

<400> 368
 ccagtgtggt ggaattcgac tcgtctcagg ccagttgcag ccttctcagc caaacgccga 60
 ccaaggaaaa ctactacca tgagaattgc agtgatttgc ttttgccctc taggcatcac 120
 ctgtgccata ccagttaaac aggctgattc tggaagtctt gaggaagaag agctttacaa 180
 caantaccca gatgctgtgg ccacatggct aaaccctgac ccatctcaga agcagaatct 240
 octagcccca cagaatgctg tgtcctctga agaaaccaat gacttttaac aagagaccct 300
 tccaagtaag tccaacgaaa gccatgacca catggatgat atggatgatg aagatgatga 360
 tgaccatgtg gacagccagg actccattga ctcgaaacgac tctgatgatg tagatgacac 420
 tgatgattct caccagtctg atgagtctca ccattctgat gaatctgatg aactggtcac 480
 tgattttccc acggacctgc cagcaaccga agttttcact ccagttgtcc ccacagtaga 540
 cacatatgat ggccgagg 558

<210> 369
 <211> 1021
 <212> DNA
 <213> Homo sapiens

<400> 369
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 ggagatgata gctagggaaa taaggatatc tgtgagtatt tataacaaaa tattttaaaat 120
 ttaaaaagaa taagaaacat caattggctt tttgtaactt aaaagagact aaccaagtgt 180
 tgtttccag ttctgtacaa gcagaggcca caggaggatt cttacataag aagcacaggg 240
 aaaagaattg ttaattctgc gtgtgtgttt ttgtttctca gaattgtttg gaagaacttt 300
 gtccagtcag aaatgagtaa aaacaagatg taagaaacat taaaacaggg ggcataatgt 360
 cttaagagat aatcttggag aatatagcaa aagacaaatt gctccattag atattataat 420
 ttggtatgta acatgaacat ttaaaattct gattaaagtg actaaaaggg tttgtttttt 480
 aaaaaaatc aaaacagaac ttacgggata aaactcaaaa taaatttact ctcatgtaga 540
 acttgatgta ggaatataag tcctctcact ttgataaaca tgaatataaa atattgctgt 600
 ctgtattcta gggtttccta cattttctgt aaagagtgat tcatgctatg tcatatgtaa 660
 atgactcaac attttgagct aaaaggctgt tcacaatata cacattcttt acttacaagg 720
 caaaataagc ttaacacctt tatattaaaa acccgggata cagcaggatt agtagcaccg 780

129

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tgaaaaataa ttcttccac aaactgcagt cttttatatt actcaatgtg actotttctct 840
taattgaatt tttaatgtac catttttagta actgggcaaa atatataatt ttcatcttat 900
aattcttggg gaaagtcatt ctggacccaa aaagtaaatt cacttcocta tttcttttagt 960
agaaaaataa tagagacttt gctctggcgc attgctgagg tacatctgaa tcttcatggt 1020
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<210> 370
<211> 204
<212> DNA
<213> Homo sapiens

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<220>
<221> misc_feature
<222> (1)...(204)
<223> n = A,T,C or G

```

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<400> 370
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attgaaggca ttccattttct aaagcttatt tagccgggtgc ttctaaagaa ttccacacta 120
acgtgataac atgggtttttg taacaataaa tgtaggatat ttctgggcac atgcaaataa 180
acctaatacat tgtttcttta aaaa                                204

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<210> 371
<211> 628
<212> DNA
<213> Homo sapiens

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<400> 371
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ttggaaaaca atatttatag ggcttaaagc ccattttcat ttctaatacta aattatgtgt 180
gcctatctga aaacttttggg ctctttcttg tttctttccc aaaattcaga agttaatggg 240
cttttatggt tttctatatt ttttttattt caatgatatt gcctgtctat gttaggctaa 300
aaaataacct tgtgtatgct accaacttaa agtgcattat tttgtgtcac tttttttttt 360
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tacctaggat atttccaagg actgccacaa aaccatattg tgcagtactt tactactttg 480
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gttctgtgta cgttattgta gttcccagtt taatatagtt ctttgtatct cttaacaggg 600
tggaagttat tgcaaaacac tctggaaa                                628

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```

<210> 372
<211> 473
<212> DNA
<213> Homo sapiens

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<400> 372
ccagtgtggt ggaattcctg ccgccctgcc gccctgccgc cctgccgccg gtggctcgtg 60
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ctacaacatg ttgggcatga tcaagaactc gctgttcgga agcgtagaga cgtggccttg 180
gcaggtccta agcaaagggg acaaggaaga agttgcctat gaagaaaggg cctgtgaagg 240
cggcaaattt gccacagtag aagtgcacga taagcctgtg gatgaggctc tacgggaagc 300
aatgcccaag gtcgcaaagt atgcaggggg caccaatgac aaggggaattg ggatggggat 360
gacagtcctt atttcctttg ctgtgttccc caatgaagat ggctctctgc agaagaaatt 420
aaaagtctgg ttccggattc caaaccaatt tcaaagcgac ccaccagctc cca                                473

```

```

<210> 373
<211> 283
<212> DNA
<213> Homo sapiens

```

130

<220>
<221> misc_feature
<222> (1)...(283)
<223> n = A,T,C or G

<400> 373
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ttttagaaaa tcagttttta gtgaccana tgcctggaga aaagctgcca ggatttttct 180
ggtctatcgc agaattttct acatcaatga gaaggatgct gcataatctt gctgtattat 240
ttcctaccgn gagaaaagaa acttaatatata tggaaacatgc ttt 283

<210> 374
<211> 529
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(529)
<223> n = A,T,C or G

<400> 374
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tggactcagg aagccggagt cgcaggaggc ggcgcctta tcaggaccat gcggccgacg 120
ggtcatcacg tcgcgcacg tgggtggaga ggacgccgaa ctccggcggt ggccgtggca 180
ggggagcctg cgcctgtggg attcccaagt atgcggagt agcctgctca gccaccgctg 240
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ccagtttggc cagctgactt ccatgccatc cttctggagc ctgcaggcct actacaccg 360
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tgccttgggt aagctgtctg cacctgtcac ctacactaaa cacatccagc ccatctgtct 480
ccaggccttc acatttgagt ttgagaaccg gacagactgc tgggtgact 529

<210> 375
<211> 519
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(519)
<223> n = A,T,C or G

<400> 375
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cataccacaa gagaagttaa tttcttaaca ttgtgttcta tgattatttg taagaccttc 120
accaagttct gatattttt aaagacatag ttcaaaattg cttttgaaaa tctgtattct 180
tgaaaatata cttgttgtgt attaggtttt taaataaccag cttaaaggatt acctcactga 240
gtcatcagta cctcctatt cagctcccca agatgatgtg tttttgctta ccctaagaga 300
ggttttcttc ttatttttag ataattcaag tgcttagata aattatgttt tctttaagtg 360
tttatggtaa actcttttaa agaaaattta atatgttata gctgaatctt tttggtaact 420
ttaaatcttt atcatagact ctgtacatat gttcaaatga gctgcttgcc tgatgtgtgt 480
atcatcggtg ggatgacaga acaaacatat ttatgatca 519

<210> 376
<211> 171
<212> DNA
<213> Homo sapiens

131

<400> 376
tcaagatttta gccaaaggctg tggcaaagggt gtaacttgta aacttgagtt ggagtactat 60
atttacaaat aaaattggca ccatgtgcca tctgtacata ttactgttgc atttactttt 120
aataaagcctt gtggcccccctt ttactttttt atagcttaaa aaaaaaaaaa a 171

<210> 377
<211> 270
<212> DNA
<213> Homo sapiens

<400> 377
ccagtgtggt ggaattaatc aggcctccca aatttagcag gtgctgggga ggaccctagg 60
gagtggtttta tgggggctag ctgggtgaaac tgccctttcc tttctgttct atgagtgtga 120
tggtgttttga gaaaatgtgg ggctatgggt caggcgact tcacatgtgc aaagatggag 180
aaagcactca cctacacgtt taggctcaga atattgattg aaacattttg aatgatcaaa 240
aataaaatgt tattttttaa gtttcaaaaa 270

<210> 378
<211> 416
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(416)
<223> n = A,T,C or G

<400> 378
ccagtgtggt ggaattcgcc actgctaggg ttacacaggtc atccctggat taaataagtg 60
atattgtggt ttttttttct ttgacacaaa gtaaaattat aattaatatt gaataaagta 120
aaaatgaact ccagtgnngn ggaattcgcc actcaggaaa tattagttgc atgaacgaag 180
gctgcatttt catcanaaca acatgcagtt caacccttcc atgtttcaat gaggggttcan 240
atncccanag ggctatgcta tcatcctgga gccactctg ctaacaatta gcanaacgga 300
agccttaatt tccanattct agtgaacttg atgagtcaan actattgcaa ttggaaatct 360
gttctcctct gctgctgcat tccctgctta atactcaagc canaaaccag gaaggt 416

<210> 379
<211> 576
<212> DNA
<213> Homo sapiens

<400> 379
ttcctatgat cattaaactc attctcaggg ttaagaaagg aatgtaaatt tctgcctcaa 60
tttgtacttc atcaataagt ttttgaagag tgcagatttt tagtcaggtc ttaaaaaataa 120
actcacaaat ctggatgcat ttctaaattc tgcaaatggt tcctgggggtg acttaacaag 180
gaataatccc acaatatacc tagctaccta atacatggag ctgggggtca acccactgtt 240
tttaaggatt tgcgcttact tgtggctgag gaaaaataag tagttcgagg aagtagtttt 300
taaagtgtgag cttatagata gaaacagaat atcaacttaa ttatgaaatt gttagaacct 360
gttctcttgg atctgaatct gattgcaatt actattgtac tgatagactc cagccattgc 420
aagtctcaga tatcttagct gtgtagtgat tcttgaaatt ctttttaaga aaaattgagt 480
agaaagaaat aaaccctttg taaatgaggc ttggcctttt tgaaagatca tccgcaggct 540
atgttaaaag gattttagct cactaaaagt gtaata 576

<210> 380
<211> 347
<212> DNA
<213> Homo sapiens

132

<400> 380

```

ccagtgtggt ggaattcggg gagaaggaag cctggggccc agccgaggaa gcgaaaaacc 60
aaacaagcag ttcccattgt ggaaccccaa gaacctgaga tcaaactaaa atatgccacc 120
cagccactgg ataaaactga tgccaagaac aagtcttttt acccttacat ccatgtagta 180
aataagtgtg aacttggagc cgtttgtaca atcatcaatg ctgaggaaga agaacagacc 240
aaattagtga ggggcaggaa gggtcagagg tcaactgaccc ctccacctag cagcactgaa 300
agcaaggcgc tcccggcctc gtcctttatg ctgcagggac ctgttgt 347

```

<210> 381

<211> 258

<212> DNA

<213> Homo sapiens

<400> 381

```

gacaagctcc tggctcttgag atgtcttctc gttaaggaga tgggcctttt ggaggtaaag 60
gataaaatga atgagttctg tcatgattca ctattctaga acttgcataa cctttactgt 120
gttagctctt tgaatgttct tgaaatttta gactttcttt gtaaacaaat gatatgtcct 180
tatcattgta taaaagctgt tatgtgcaac agtgtggaga ttccttgtct gatttaataa 240
aataacttaaa cactgaaa 258

```

<210> 382

<211> 580

<212> DNA

<213> Homo sapiens

<400> 382

```

gccgtaggga gtacctgctg cccagctga ctgtggcccc ctccgtgata catccatctc 60
cagggagcaa gacagagacg caggaatgga aagcggagtt cctaacagga tgaaagtacc 120
cccacagatt cccccagtac ctccaagcaa gtagctttcc acatttgtca cagaaatcag 180
aggagagatg gtgttgggag ccctttggag aacgccagtc tcccaggccc cctgcatcta 240
tcgagtttgc aatgtcacaa cctctctgat ctgtgtctca gcatgattct ttaatagaag 300
ttttatTTTT tctgtcactc tgctaatacat gtgggtgagc cagtggaaaca gcgggagacc 360
tgtgctagtt ttacagattg cctcctaata acgcggctca aaaggaaacc aagtggctag 420
gagttgtttc tgacccactg atctctacta ccacaaggaa aatagtttag gagaaaccag 480
cttttactgt ttttgaaaaa ttacagcttc accctgtcaa gtttaacaagg aatgcctgtg 540
ccaataaaaag gtttctccaa cttgaagtct actctgaaaa 580

```

<210> 383

<211> 608

<212> DNA

<213> Homo sapiens

<400> 383

```

gtgctagatg aaaagcgtgc aatatgyttt aaagctatca aaaaaaactg aatattataa 60
gcaagcaata tcatagtaat tggcagatta gctcatattc tatacagcat cgtttaaata 120
ggaaaaatTTT aatgctagca aaaaataaat ttagaaatat ggcatgacat gaaaatacaa 180
tcttatatTTT acaccagctt ttcactaata ttttgtaact aaggtgatgg ggaactccat 240
tcagataata aaattctctt tcagctagag aagttaacag gaataaatat atgaacaaaa 300
aagctgcaag gataaatgtg gagaaaatga tgagaattag ctaacatttt taagtttttt 360
taaactttct tcccctcact tagttgtact taatatTTT taggaaagtaa taattttttt 420
aatTTTctat caactaatag tatagtaact atgattaact tgtttacttt ttctgaggat 480
tagtaaatca atTTTTTTTT tatttcaaat ttttggaatt acacttgagg gtaaatTTTaa 540
tctggtaaac tgaatttctc agttaaataa aattagttgc agtatatgat gaacagtgtg 600
tgactcaa 608

```

<210> 384

<211> 585

<212> DNA

<213> Homo sapiens

133

```

<400> 384
ttatttcctt aaatattgct acaaaaggaa gatgcgggtg taagccctga tttttttttc 60
tcccaagaaa aatcttaaag gaccacttta gataatattt gattcctact gtaaaattta 120
gaaaatgatg aattcttgct catttttgta atcaagattt taggaaaaac agaagtacat 180
ctatctttat gaaattttgg gcagggtttt gtgtatcaat attttgtagt tttagggaat 240
attttatttt tttagttatt gtgtcaaatt ataattataa aaggtacagc agaaaatata 300
ccatgttttt atataggttc acacctgtac ttaggaggga ccctgtccat ctatatactt 360
tttgatataa attttaaaat gttaaagatc cacaaggtct taataaaatg attctatagc 420
tagaaaaaca tttaacctcc cagtgttttg cactaaaata tactgtgaaa ggaaactaga 480
aagactgtaa ctattgctgg aaatgttcta tattgaatgt acatgctctt gttggaaaaa 540
tgtctatatg tgatggaaat aaaccagaat cgaagttatt tcaaa 585

```

```

<210> 385
<211> 511
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(511)
<223> n = A,T,C or G

```

```

<400> 385
atattgtaca gtatttatcg agataaacat ggtwatcaaa atgtccattg tttataagct 60
gagaatttgc caatatTTTT caaggagagg ctctctgctg aattttgatt ctgcagctga 120
aatttaggac agttgcaaac gtgaaaagaa gaaaattatt caaatttga cattttaatt 180
gtttaaaaaat tgtacaaaag gaaaaaatta gaataagtag tggcgaacca tctctgtgg 240
cttgtttaaa aagggcaaaa gttttagact actaaatttt ttaacagtaa gttataaaat 300
ttagtagtct aaaacttata acttactgtt aaaagcaaaa atggccatgc aggttgacac 360
cgttggtaat ttataatagc ttttgttcga tcccaacttt ccattttgtt cagataaaaa 420
aaaccatgaa attactgngt ttgaaatatt ttcttatggt ttgtaaatatt tctgtaaatt 480
tattgtgata ttttaaggnt ttccccctt t 511

```

```

<210> 386
<211> 311
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(311)
<223> n = A,T,C or G

```

```

<400> 386
gtggaattcc atgaatntag ttcccatcat gacttanaag gtgctgtagg tgggtactac 60
ccagaaccca gtnagctttg tcaacttgat caaagtgatt ctgatttcca tggagatctt 120
acatttcaac acgtatttca taaccacact taccatttac agccaactgc accagaatct 180
acttctgaac cttttccgtg gcctgggaag tcacagaaga taaggagtag ataccttgaa 240
gacacagata gaaacttgag ccgtgatgaa cagcngctca aagctttgca tatccctttt 300
tctgtagatg a 311

```

```

<210> 387
<211> 461
<212> DNA
<213> Homo sapiens

```

```

<400> 387
-cacagatagc aagacttcat ttcaggagtt gggagtggga agtaggaagt gtttaatccc 60

```


134

```

aagtttttggg gccctaaaat ggctagtagt atagttaatt ctcaattctc tagctgtgat 120
cttctgtgcc ttctatctct tcctaaggaa aaccacatta gatgaacca gggctcagtc 180
attttaggga gaggggttgag acaacactgc cagcaacaca gctggaatca cccgagtcgg 240
gaacattaaa gttcctgaga gaatatgaaa caactatcaa cataatattt ctccctactt 300
ttacagtaaa atattggaag taaataaata tagggaatgc aacaactggc taggagtggt 360
ttacattcag ttgtttggaa gcataacaca ttcagctcct ttgaatcttc ccgttagaaa 420
atacagaatt actctatcac cttttaagggt acagtaaaaa a 461

```

<210> 388

<211> 555

<212> DNA

<213> Homo sapiens

<400> 388

```

ggataaaggc cagggatgct gctcaacctc ctaccatgta caggacgtct cccattaca 60
actacccaat ccgaagtgtc aactgtgtca ggactaagaa accctgggtt tgagtagaaa 120
agggcctgga aagaggggag ccaacaaatc tgtctgtctc ctcacattag tcattggcaa 180
ataagcattc tgtctctttg gctgctgcct cagcacagag agccagaact ctatcgggca 240
ccaggataac atctctcagt gaacagagtt gacaaggcct atgggaaatg cctgatggga 300
ttatcttcag cttgttgagc ttctaagttt ctttcccttc attctaccct gcaagccaag 360
ttctgtaaga gaaatgcctg agttctagct cagggttttct tactctgaat ttagatctcc 420
agacccttcc tggccacaat tcaaattaag gcaacaaaca tataccttcc atgaagcaca 480
cacagacttt tgaaagcaag gacaatgact gcttgaattg aggccttgag gaatgaagct 540
ttgaaggaaa agaatt 555

```

<210> 389

<211> 563

<212> DNA

<213> Homo sapiens

<400> 389

```

ttattttggg cagctgagta ccatcaggat atttaaccct ttaagtgtg ttttgggagt 60
agaaaactaa agcaacaata cttcctcttg acagctttga ttggaatggg gttattagat 120
cattcacctt ggtcctacac tttttaggat gcttggtgaa cataacacca cttataatga 180
acatccctgg ttcctatatt ttgggctatg tgggtaggaa ttgttacttg ttactgcagc 240
agcagcccta gaaagtaagc ccagggtctc agatctaagt tagtccaaaa gctaaatgat 300
ttaaagtcaa gttgtaatgc taggcataag cactctataa tacattaaat tataggccga 360
gcaatttagg aatgtttctg aaacattaaa cttgtattta tgtcactaaa attctaacac 420
aaacttaaaa aatgtgtctc atacatatgc tgtactaggc ttcacatcatg atttctaaat 480
ttgtgtatga tttgaatata tgaaagratt tatacaagag tgttatttaa aattattaaa 540
aataaatgta tataatttga aaa 563

```

<210> 390

<211> 278

<212> DNA

<213> Homo sapiens

<400> 390

```

gaacattatg ttttagatgg gtagtactag ctactcatct gtccccaga aaccaagct 60
aagcatggac atattgaaga gaatgtcagc accattaaaa aaactctaga aaaatcacat 120
gtgatgactg aggttaattc agtctgtcaa ttacatcagt ataattgcct tcttgaacc 180
ctaagtatgg tgaagcagaa ttgaattcta caaagtcctt tcatctgttt tcctatggaa 240
taattaacaa acccaataaa tgtataaata gcatgaaa 278

```

<210> 391

<211> 578

<212> DNA

<213> Homo sapiens

135

<400> 391

```

cggcgctcgg ctgcaggat ggatcccgt cccgggacag actcggcgcc gctggctggc 60
ctggcctggg cgtcggcctc tgcacccccg ccgcgggggg tcagcgcgat ctctgcacc 120
gtcagagggg caccgcag ctttggaag agcttcgcgc agaaatctgg ctacttcctg 180
tgccttagtt ctctgggcag cctagagaac ccgcaggaga acgtggtggc cgatatccag 240
atcgtgggtgg acaagagccc cctgccgctg ggcttctccc ccgtctgcga cccatggat 300
tccaaggcct ctgtgtccaa gaagaaacgc atgtgtgtga agctgttgcc cctgggagcc 360
acggacacgg ctgtgtttga tgtccggctg agtgggaaga ccaagacagt gcctggatac 420
cttcgaatag gggacatggg cggctttgcc atctggtgca agaaggccaa ggccccgagg 480
ccagtgcaca agccccgagg tctcagccgg gacatgcagg gcctctctct ggatgcagcc 540
agccagccaa gtaagggcgg cctcctggag cggacagc 578

```

<210> 392

<211> 439

<212> DNA

<213> Homo sapiens

<400> 392

```

ttcaacaaac cttgtatagt gtatgttttg ccatatttaa tattaatagc agaggaagac 60
tccttttttc atcactgtat gaatttttta taatgttttt ttaaaatata tttcatgtat 120
acttataaac taattcacac aagtgtttgt cttagatgat taaggaagac tatatctaga 180
tcatgtctga ttttttattg tgacttctcc agccctggtc tgaatttctt aaggttttat 240
aaacaaatgc tgctatttat tagctgcaag aatgcacttt agaactattt gacaattcag 300
actttcaaaa taaagatgta aatgactggc caataataac catttttagga aggtgttttg 360
aattctgtat gtatatattc actttctgac atttagatat gccaaaagaa ttaaaatcaa 420
aagcactaag aaataaaaa 439

```

<210> 393

<211> 544

<212> DNA

<213> Homo sapiens

<400> 393

```

tttgaattta caccaagaac ttctcaataa aagaaaatca tgaatgctcc acaatttcaa 60
cataaccaca gagaagttaa tttcttaaca ttgtgttcta tgattatttg taagaccttc 120
accaagtctt gatattcttt aaagacatag ttcaaaattg cttttgaaaa tctgtattct 180
tgaaaatata cttgttgtgt attaggtttt taaataccag cttaaaggatt acctcactga 240
gtcatcagta ccctcctatt cagctcccca agatgatgtg tttttgotta ccctaagaga 300
ggttttcttc ttatttttag ataattcaag tgcttagata aattatgttt tctttaagtg 360
tttatggtaa actcttttaa agaaaattta atatgttata gctgaatctt tttggtaact 420
ttaaatcttt atcatagact ctgtacatat gttcaaatta gctgcttgcc tgatgtgtgt 480
atcatcggtg ggatgacaga acaaacatat ttatgatcat gaataatgtg ctttgtaaaa 540
agat 544

```

<210> 394

<211> 424

<212> DNA

<213> Homo sapiens

<400> 394

```

aaacatcatt tagcagcaat gaacctgtca acacatggaa ataaggttta cagtcatgca 60
aatgtccatt taactttgtt tgagccaaac aaatataaca gtaaaactaat tagactggct 120
tacatccccg tagacagtga aaccaattat ttcttaaaga agggtttgct tgtttttact 180
ctagggcaaa ggtgcataac ttcttgaat actcctgaat agttcttcaa atcaggacag 240
ataaagtttg caactgatgg aatagctacc ttgatgtgca aatggttggg tctttaatta 300
ggtttcattta tataattgag aaagaagcca gggaatgcat ttgtgcaagg atgattttta 360
aagaagaggg atgggtctgcc ttttaattct gtatgggagg aaaattcata aaaaactgaa 420
aaaa 424

```

136

<210> 395
 <211> 279
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(279)
 <223> n = A,T,C or G

<400> 395
 ttctctatgat nattaaactc attctcaggg ttaagaaagg aatgtaaatt tctgcctcaa 60
 tttgcacttc atcaataagt ttttgaagag tgcagatttt tagtcaggtc ttaaaaaataa 120
 actcacaaat ctggatgcat ttctaaattc tgcaaatgtt tcctgggggtg acttaacaag 180
 gaataatccc acaatatacc tagctaccta atacatggag ctgggggtca acccactgtt 240
 ttttaaggatt tgcgcttact tgtggctgan gaaaaataa 279

<210> 396
 <211> 3293
 <212> DNA
 <213> Homo sapiens

<400> 396
 cagccccggg ccaggccgcg gccggggcag gagcgcaggg gctttgttat gcacctaaag 60
 ccatattgga agctccagaa gaaagagcac cccccggaag tcagcaggga aacgcagaga 120
 actcctatga accacaaaaa ggctgtaaat gatgaaacat gcaaagctag ccacataaca 180
 tcaagtgtct ttcttcagc ctctctcggg aaagcatcat ctcgaaagcc atttgggatc 240
 ctttctccaa atgttctgtg cagtatgagt ggaagagtc ctgtagagag cagcttgaat 300
 gttaaaacca aaaagaatgc accatctgca acgatccacc agggcggaaga agaaggacca 360
 cttgatatct gggctgttgt gaaacctgga aataccaagg aaaaaattgc attctttgca 420
 tcccaccagt gtagtaacag gataggatct atgaaaaataa aaagtccctg ggatattgat 480
 gggagagcta ctaagagaag gaaaaaatca ggggatctta aaaaagccaa ggtacagggtg 540
 gaaaggatga gggagggttaa cagcagggtgc taccacacctg agccttttgc atgtggcatt 600
 gagcactgtt ctgtgcacta tgtgagtgac agtggggatg gagtctatgc tgggaggcct 660
 ctgtcagtta tacagatggg tgccttcttg gagcaaagag ccagtgtctt gctagctagc 720
 tgttcaaaaa actgcacaaa ctcacctgca attgtgaggt tttctggcca atccagaggt 780
 gtgcctgcag tgtctgagtc ctattctgcc ccaggagctt gtgaagaacc cacagaaagg 840
 ggaaatcttg aggttggtga accacagagc gaaccagtcc gtgtccttga catggtagcc 900
 aagttggagt ctgagtgcct gaagcggcag ggccagcgtg agcctgggag cctctcaagg 960
 aataacagct tccgtcgaaa tgtgggcaga gtattgcttg caaatagcac tcaggctgat 1020
 gaaggcaaaa caaagaaagg cgtcttgagg gcacctgaca ctccaggtgaa tcctgtgggg 1080
 tctgtatctg tggattgttg cccttcaaga gctgatcggt gttctcctaa ggaggaccag 1140
 gccctgggag gtgcttctca ggactgcccc ccattgccag caggagttag tttccacata 1200
 gacagtgcag agttagagcc gggttcgcaa actgocgtga aaaacagcaa cagatatgat 1260
 gtggaaatga cagatgaact cgttgggtta cctttttcct ctcataccta ttcccaagcc 1320
 tctgaattgc ccacagatgc tgttgattgt atgagcagag agcttgtgtc ccttactagc 1380
 cgaaatcctg atcaaagaaa agaatctttg tgcattagta tcaactgtgtc caaggtagac 1440
 aaagaccagc cttccatttt aaactcctgt gaagaccag ttccagggat gttgtttttt 1500
 ttgccacctg gtcagcactt gtcagactat tcccagttga atgaaagcac aacaaaagag 1560
 tottcagagg ccagccagct tgaagatgct gctgggggtg acagtgcac tgaggaaaaa 1620
 agtgggtctg ctgagccatt tgtactgcca gcctcttctg tggaaagtac attaccagt 1680
 cttgaggcat ccagttggaa gaagcagggt tgcgatgact tcctggagac caggtttaaa 1740
 atccagcagc ttttggagcc tcagcagtac atggcttttc tgccccacca cattatggta 1800
 aaaatcttca ggttacttcc caccaagagt ttagtggccc ttaaattgtac ctgctgctat 1860
 ttcaagttta tcattgagta ctacaatatc aggccagcag attctcgtct gggttcgagat 1920
 ccacgctata gagaggatcc ttgcaaacag tgcaagaaaa agtatgtgaa aggggatgtg 1980
 tccctgtgcc gatggcacc caagccctat tgccagcgtat gccagggtat 2040
 tggatgtgct gccaccgggc tcagaaagga ttccctggct gtaagctggg gcttcatgac 2100

<213> Homo sapiens

Gln	Pro	Arg	Ala	Arg	Pro	Arg	Pro	Gly	Gln	Glu	Arg	Arg	Gly	Phe	Val
Met	His	Leu	Lys	Pro	Tyr	Trp	Lys	Leu	Gln	Lys	Lys	Glu	His	Pro	Pro
Glu	Val	Ser	Arg	Glu	Thr	Gln	Arg	Thr	Pro	Met	Asn	His	Gln	Lys	Ala
Val	Asn	Asp	Glu	Thr	Cys	Lys	Ala	Ser	His	Ile	Thr	Ser	Ser	Val	Phe
Pro	Ser	Ala	Ser	Leu	Gly	Lys	Ala	Ser	Ser	Arg	Lys	Pro	Phe	Gly	Ile
Leu	Ser	Pro	Asn	Val	Leu	Cys	Ser	Met	Ser	Gly	Lys	Ser	Pro	Val	Glu
Ser	Ser	Leu	Asn	Val	Lys	Thr	Lys	Lys	Asn	Ala	Pro	Ser	Ala	Thr	Ile
His	Gln	Gly	Glu	Glu	Glu	Gly	Pro	Leu	Asp	Ile	Trp	Ala	Val	Val	Lys
Pro	Gly	Asn	Thr	Lys	Glu	Lys	Ile	Ala	Phe	Phe	Ala	Ser	His	Gln	Cys
Ser	Asn	Arg	Ile	Gly	Ser	Met	Lys	Ile	Lys	Ser	Ser	Trp	Asp	Ile	Asp
Gly	Arg	Ala	Thr	Lys	Arg	Arg	Lys	Lys	Ser	Gly	Asp	Leu	Lys	Lys	Ala
Lys	Val	Gln	Val	Glu	Arg	Met	Arg	Glu	Val	Asn	Ser	Arg	Cys	Tyr	Gln
Pro	Glu	Pro	Phe	Ala	Cys	Gly	Ile	Glu	His	Cys	Ser	Val	His	Tyr	Val
Ser	Asp	Ser	Gly	Asp	Gly	Val	Tyr	Ala	Gly	Arg	Pro	Leu	Ser	Val	Ile
Gln	Met	Val	Ala	Phe	Leu	Glu	Gln	Arg	Ala	Ser	Ala	Leu	Leu	Ala	Ser
Cys	Ser	Lys	Asn	Cys	Thr	Asn	Ser	Pro	Ala	Ile	Val	Arg	Phe	Ser	Gly

138

Gln Ser Arg Gly Val Pro Ala Val Ser Glu Ser Tyr Ser Ala Pro Gly
 260 265 270
 Ala Cys Glu Glu Pro Thr Glu Arg Gly Asn Leu Glu Val Gly Glu Pro
 275 280 285
 Gln Ser Glu Pro Val Arg Val Leu Asp Met Val Ala Lys Leu Glu Ser
 290 295 300
 Glu Cys Leu Lys Arg Gln Gly Gln Arg Glu Pro Gly Ser Leu Ser Arg
 305 310 315 320
 Asn Asn Ser Phe Arg Arg Asn Val Gly Arg Val Leu Leu Ala Asn Ser
 325 330 335
 Thr Gln Ala Asp Glu Gly Lys Thr Lys Lys Gly Val Leu Glu Ala Pro
 340 345 350
 Asp Thr Gln Val Asn Pro Val Gly Ser Val Ser Val Asp Cys Gly Pro
 355 360 365
 Ser Arg Ala Asp Arg Cys Ser Pro Lys Glu Asp Gln Ala Trp Asp Gly
 370 375 380
 Ala Ser Gln Asp Cys Pro Pro Leu Pro Ala Gly Val Ser Phe His Ile
 385 390 395 400
 Asp Ser Ala Glu Leu Glu Pro Gly Ser Gln Thr Ala Val Lys Asn Ser
 405 410 415
 Asn Arg Tyr Asp Val Glu Met Thr Asp Glu Leu Val Gly Leu Pro Phe
 420 425 430
 Ser Ser His Thr Tyr Ser Gln Ala Ser Glu Leu Pro Thr Asp Ala Val
 435 440 445
 Asp Cys Met Ser Arg Glu Leu Val Ser Leu Thr Ser Arg Asn Pro Asp
 450 455 460
 Gln Arg Lys Glu Ser Leu Cys Ile Ser Ile Thr Val Ser Lys Val Asp
 465 470 475 480
 Lys Asp Gln Pro Ser Ile Leu Asn Ser Cys Glu Asp Pro Val Pro Gly
 485 490 495
 Met Leu Phe Phe Leu Pro Pro Gly Gln His Leu Ser Asp Tyr Ser Gln
 500 505 510
 Leu Asn Glu Ser Thr Thr Lys Glu Ser Ser Glu Ala Ser Gln Leu Glu
 515 520 525
 Asp Ala Ala Gly Gly Asp Ser Ala Ser Glu Glu Lys Ser Gly Ser Ala
 530 535 540
 Glu Pro Phe Val Leu Pro Ala Ser Ser Val Glu Ser Thr Leu Pro Val
 545 550 555 560
 Leu Glu Ala Ser Ser Trp Lys Lys Gln Val Ser His Asp Phe Leu Glu
 565 570 575
 Thr Arg Phe Lys Ile Gln Gln Leu Leu Glu Pro Gln Gln Tyr Met Ala
 580 585 590
 Phe Leu Pro His His Ile Met Val Lys Ile Phe Arg Leu Leu Pro Thr
 595 600 605
 Lys Ser Leu Val Ala Leu Lys Cys Thr Cys Cys Tyr Phe Lys Phe Ile
 610 615 620
 Ile Glu Tyr Tyr Asn Ile Arg Pro Ala Asp Ser Arg Trp Val Arg Asp
 625 630 635 640
 Pro Arg Tyr Arg Glu Asp Pro Cys Lys Gln Cys Lys Lys Lys Tyr Val
 645 650 655
 Lys Gly Asp Val Ser Leu Cys Arg Trp His Pro Lys Pro Tyr Cys Gln
 660 665 670
 Ala Leu Pro Tyr Gly Pro Gly Tyr Trp Met Cys Cys His Arg Ser Gln
 675 680 685
 Lys Gly Phe Pro Gly Cys Lys Leu Gly Leu His Asp Asn His Trp Val
 690 695 700
 Pro Ala Cys His Ser Phe Asn Arg Ala Ile His Lys Lys Ala Lys Gly
 705 710 715 720
 Thr Glu Ala Glu Glu Glu Tyr

139

725

<210> 398
 <211> 403
 <212> DNA
 <213> Homo sapiens

<400> 398
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 cactatgtcg ggtggcctcc tgaaggcgct ggcgagcgac tcctacgtgg agctgagcca 120
 gtaccgggac cagcacttcc ggggtgacaa tgaagaacaa gaaaaattac tgaagaaaag 180
 ctgtacgtta tatgttgga atctttcttt ttacacaact gaagaacaaa tctatgaact 240
 cttcagcaaa agtgggtgaca taaagaaaat cattatgggt ctggataaaa tgaagaaaac 300
 agcatgtgga ttctgttttg tggaaatatta ctcacgcgca gatgcggaaa acgccatgcg 360
 gtacataaat gggacgcgctc tggatgaccg aatcattcgc aca 403

<210> 399
 <211> 403
 <212> DNA
 <213> Homo sapiens

<400> 399
 ttttgatgct ttctttcatg ggaatagtca cttttttatt tagtaaatcg cattgctgga 60
 accaccaagg agtgtggaat gtctttgagt gtattattta tgcaagtcac agtcacgttg 120
 ccatcatggc agctatgtga aacactaata aatgtgtttt tactttttat tcccgtaaaa 180
 actgatgtaa aacaggataa aggtttgtta tagtcaacta taagtatctg ggtctaagta 240
 atttccttag atgtttctaa agaaacattt tcagctttgc tcccattatg attccaataa 300
 ggaacgcttt cctagtgcga ttttaggagt aaagtttgaa gagataaaaa tagccaaaga 360
 taggagacgt ctgaattttg aatgataaac agtgaatgtt taa 403

<210> 400
 <211> 283
 <212> DNA
 <213> Homo sapiens

<400> 400
 ttatttttcc cctcaaattc atgattttta cgtctgttac aaagggaatt ttgctgatag 60
 ctctttgggt cccactgttc cattttatgc taatagattc cattctaggg ccagccgctc 120
 tcttgactga tgggtgttccc ttttaaccctt ggcattgata atagaatttt ggtgaatgaa 180
 agaaccctaa taggccagat agtccccca ggccctgata tccataaaa gcttggaat 240
 gcattatgta attgtcctta gtctttttgt tgttttagaa aaa 283

<210> 401
 <211> 303
 <212> DNA
 <213> Homo sapiens

<400> 401
 cataaagggt gtgcgcgtct tcgacgtggc ggtcttggcg ccaactgctgc gagaccggc 60
 cctggacctc aagggtcatcc acttggtgcg tgatccccgc gcggtggcga gttcacggat 120
 ccgctcgcgc caccgcctca tccgtgagag cctacagggt gtgcgcagcc gagaccggc 180
 agctcaccgc atgcccttct tggaggccgc gggccacaag cttggcgcca agaaggagg 240
 cgtgggcggc cccgcagact accacgctct gggcgctatg gaggtcatct gcaatagtat 300
 ggc 303

<210> 402
 <211> 473
 <212> DNA

140

<213> Homo sapiens

<400> 402

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ccaacacagt cagaacatt gttttgaatc ctctgtaaac caaggcatta atcttaataa 60
accaggatcc atttaggtac cacttgatat aaaaaggata tccataatga atattttata 120
ctgcatcctt tacattagcc actaaatagc ttattgcttg atgaagacct ttcacagaat 180
cctatggatt gcagcatttc acttggctac ttcataccca tgccttaaag aggggcagtt 240
tctcaaaagc agaaacatgc cgccagttct caagttttcc tcctaactcc atttgaatgt 300
aagggcagct ggccccaat gtggggaggt ccgaacattt tctgaattcc cattttcttg 360
ttcgcggtta aatgacagtt tctgtcatta cttagattcc gatctttccc aaaggtgttg 420
atttacaag aggcagcta atagcagaaa tcatgaccct gaaagagaga tga 473

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<210> 403

<211> 513

<212> DNA

<213> Homo sapiens

<400> 403

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ggcattaact tttagaatth gggctggtga gattaattht ttttaatatc ccagctagag 60
atatggcctt taactgacct aaagaggtgt gttgtgattt aattttttcc cgttcctttt 120
tcttcagtaa acccaacaat agtctaacct taaaaattga gttgatgtoc ttataggtca 180
ctacccttaa ataaacctga agcaggtgtt ttctcttgga catactaaaa aatacctaaa 240
aggaagctta gatggtctgt gacacaaaaa attcaattac tgtcatctaa tgccagctgt 300
taaaagtgtg gccactgagc atttgatttt ataggaaaaa atagtatttt tgagaataac 360
atagctgtgc tattgcacat ctgttgaggg acatcccaga tttgcttata ctacgtgcct 420
gtgatattga gtttaaggat ttgaggcagg ggtaattatt aaacatattg cttctattct 480
tggaaaaaata gaagtgtaaa atgttaataa tac 513

```

<210> 404

<211> 533

<212> DNA

<213> Homo sapiens

<400> 404

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ccagtgtggt ggaattcgcg gtaggctggg accataacac aagcatgact atatgaagga 60
agaggaaggt tttcctgaag atgaggcgac tgaatcgga aaaaacttta agtttggtta 120
aagagttgga tgcctttccg aaggttcctg agagctatgt agagacttca gccagtgag 180
gtacagtttc tctaatagca tttacaacta tggctttatt aaccataatg gaattctcag 240
tatatcaaga tacatggatg aagtatgaat acgaagtaga caaggatttt tctagcaaat 300
taagaattaa tatagatatt actgttgcca tgaagtgtca atatgttgga ggggatgtat 360
tggaatttagc agaaacaatg gttgcatctg cagatggttt agtttatgaa ccaacagtat 420
ttgatctttc accacagcag aaagagtggc agaggatgct gcagctgatt cagagtaggc 480
tacaagaaga gcattcactt caagatgtga tattttaaaag tgctttttaa agt 533

```

<210> 405

<211> 513

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(513)

<223> n = A,T,C or G

<400> 405

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ccagnnggt ggaattcctt agacatatct tgagcctaca gcagaggaac ctccagtctc 60
agcaccatga atcaaaactgc cattctgatt tgctgcctta tctttctgac tctaagtggc 120
attcaaggag tacctctctc tagaactgta cgctgtacct gcacagcat tagtaatcaa 180
cctgtttaatc caaggtcttt agaaaaactt gaaattattc ctgcaagcca attttgtcca 240

```

141

```

cgtgttgaga tcattgctac aatgaaaaag aagggtgaga agagatgtct gaatccagaa 300
tcgaaggcca tcaagaatctt actgaaagca gtttagcaagg aaagggtctaa aagatctcct 360
taaaaccaga ggggagcaaa atcgatgcag tgcttccaag gatggaccac acagaggctg 420
cctctcccat cacttcoccta catggagtat atgtcaagcc ataattgttc ttagtttgca 480
gttacactaa aagggtgacca atcatggtca cca 513

```

<210> 406

<211> 483

<212> DNA

<213> Homo sapiens

<400> 406

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atataccatt taatacattt acacttttctt atttaagaag atattgaatg caaaataatt 60
gacatataga actttacaaa catatgtcca aggactctaa attgagactc ttccacatgt 120
acaatctcat catcctgaag cctataatga agaaaaagat ctagaactg agttgtggag 180
ctgactctaa tcaaattgtga tgattggaat tagaccattt ggcctttgaa ctttcatagg 240
aaaaatgacc caacatttct tagcatgagc tacctcatct ctagaagctg ggatggactt 300
actattcttg tttatatattt agatactgaa aggtgctatg cttctgttat tattccaaga 360
ctggagatag gcagggctaa aaagggtatta ttatttttcc tttaatgatg gtgctaaaat 420
tcttcctata aaattcctta aaaataaaga tggtttaatc actaccattg tgaaaacata 480
act 483

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<210> 407

<211> 241

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(241)

<223> n = A,T,C or G

<400> 407

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tcacaaagnc cactttactc aaattgggtga acagngnata ggaagaagcc agcaggagct 60
ctgactaagg ttgacataat angtcacact ccctattactt tgatatctga tcaaattgtat 120
agactnggct ttgttttttg tgctattagg aaattctgat gagcattact attcactgat 180
gcagaaagac gttctttttgc ataaaagact ttttttaaca ctttggactt ctctgaaata 240
t 241

```

<210> 408

<211> 213

<212> DNA

<213> Homo sapiens

<400> 408

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ccagtgtggt ggaattcaca tgatacagcc actgggctta tacagtatgc attggaccag 60
ggcgtgaacg tcacccagggt attcgtggac accgtaggga tgccagagac ataccaggcg 120
cggttgacgc aaagttttcc cgggattgag gggaccggcc aaggccaaag cagatgccct 180
ctacccgggtg gtttagtgctg ccagcatctg tgc 213

```

<210> 409

<211> 413

<212> DNA

<213> Homo sapiens

<400> 409

```

tcagatgagt ggctgctgaa ggggccccct tgtcattttc attataaacc aatttccact 60
tatttgaact cttaagtcac aaatgtataa tgacttatga attagcacag ttaagttgac 120
actagaaact gcccatctct gtattacact atcaaatagg aaacattgga aagatgggga 180

```


142

```

aaaaaatctt attttaaaat ggcttagaaa gttttcagat tactttgaaa attctaaact 240
tctttctgtt tccaaaactt gaaaatatgt agatggactc atgcattaag actgttttca 300
aagctttcct cacattttta aagtgtgatt ttccctttta tatacatatt tattttcttt 360
aaagcagcta tatcccaacc catgactttg gagatatacc tataaaacca ata 413

```

<210> 410

<211> 153

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(153)

<223> n = A,T,C or G

<400> 410

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gcaaacacag actgaagaaa gacgaaaagt gggaaataac ttgcaacgtc tgttagagat 60
ggttgctaca catgttgggt ctgtaganaa acatcttgag gagcagattc ctaaagttga 120,
taganaatat gaagaatgca tgtcaaaaga tct 153

```

<210> 411

<211> 253

<212> DNA

<213> Homo sapiens

<400> 411

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cagtgtggtg gaattcgtcg gcgaaagcgg cggaagttc gtactgggca gaacgcgacg 60
ggtctgcggc ttaggtgaaa atgcctcgtg taaaagcagc tcaagctgga agacagagct 120
ctgcaaagag acatcttgca gaacaatttg caagttggag agataataac tgacatggca 180
aaaaaggaat ggaaagtagg attaccattt ggccaaggag gctttggctg tatatatctt 240
gctgatatga att 253

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<210> 412

<211> 3079

<212> DNA

<213> Homo sapiens

<400> 412

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gaagtgaagta gtgggggtgc cagaccaggt gcgtctgccg ctggattgtg ataggaagca 60
gagtgttcgt gtgaaagatg gatactatga tgctgaatgt gcggaatctg tttgagcagc 120
ttgtgcgccg ggtggagatt ctgagtgaag gaaatgaagt ccaatttatc cagttggcga 180
aggacttttg ggatttcogt aaaaagtggc agaggactga ccatgagctg gggaaatata 240
aggatctttt gatgaaagca gagactgagc gaagtgtctt ggatgttaag ctgaagcatg 300
cacgtaatca ggtggatgta gagatcaaac ggagacagag agctgaggct gactgcgaaa 360
agctggaacg acagattcag ctgattcgag agatgctcat gtgtgacaca tctggcagca 420
ttcaactaag cgaggagcaa aaatcagctc tggcttttct caacagaggc caaccatcca 480
gcagcaatgc tgggaacaaa agactatcaa ccattgatga atctggttcc attttatcac 540
atatcagctt tgacaagact gatgaatcac tggattggga ctcttctttg gtgaagactt 600
tcaaactgaa gaagagagaa aagaggcgct ctactagccg acagtttgtt gatggtcccc 660
ctggacctgt aaagaaaact cgttccattg gctctgcagt agaccagggg aatgaatcca 720
tagttgcaaa aactacagtg actgttccca atgatggcgg gcccatogaa gctgtgtcca 780
ctattgagac tgtgccatat tggaccagga gccgaaggaa aacaggctact ttacaacctt 840
ggaacagtga ctccaccctg aacagcaggc agctggagcc aagaactgag acagacagtg 900
tgggcacgcc acagagtaat ggagggatgc gcctgcatga ctttgtttct aagacggtta 960
ttaaactgaa atcctgtgtt ccatgtggaa agcggataaa atttggcaaa ttatctctga 1020
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gcattcctac cctgatagga acacctgtca agattggaga gggaaatgctg gcagactttg 1140
tgtccagac ttctccaatg atccctcca ttgttgtgca ttgtgtaaat gagattgagc 1200
aaagaggtct gactgagaca ggctgtata ggatctctgg ctgtgaccgc acagtaaaag 1260

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143

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agctgaaaga gaaattcctc agagtgaana ctgtaccctt cctcagcaaa gtggatgata 1320
tccatgctat ctgtagcctt ctaaaagact ttcttcgaaa cctcaaagaa cctcttctga 1380
cctttcgctt taacagagcc tttatggaag cagcagaaat cacagatgaa gacaacagca 1440
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tcctcatgat ccacttgagc agagtggctc agagtccaca tactaaaaatg gatgttgcca 1560
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tgacaatgtt acaggacatc aagcgtaac ccaagggtgt tgagcgctg ctttccttgc 1680
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tgggacctgt gaccactcct gaacatcagc ttctcaagac tccttcatct agttccctgt 1860
cacagagagt ccgttccacc ctaccaaga acactcctag atttgggagc aaaagcaagt 1920
ctgccactaa cctaggacga caaggcaact tttttgcttc tccaatgctc aagtgaagtc 1980
acatctgcct gttacttccc agcattgact gattagaaga aaggacacat ctgtactctg 2040
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aattgtgcat gaggggtttt ttaaaactat atatatctcc ccttccttct cctcaagtca 2160
cataatatca gcactttgtg ctggtcattg ttgggagctt ttagatgaga catctttcca 2220
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tctaagaacc agaagttctc attccccatt atgaactgag ctataatatg gagctttcat 2520
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gcactttgga tgctgaaatt tttcccatgg aacatagcca catctagata gatgtgagct 2940
ttttcttctg ttaaaattat tcttaatgtc tgtaaaaacg attttcttct gtagaatgtt 3000
tgacttcgta ttgaccctta tctgtaaaac acctatttgg gataaatattt ggaaaaaagt 3060
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<210> 413

<211> 632

<212> PRT

<213> Homo sapiens

<400> 413

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Met Asp Thr Met Met Leu Asn Val Arg Asn Leu Phe Glu Gln Leu Val
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                    20                      25                      30
Leu Ala Lys Asp Phe Glu Asp Phe Arg Lys Lys Trp Gln Arg Thr Asp
                    35                      40                      45
His Glu Leu Gly Lys Tyr Lys Asp Leu Leu Met Lys Ala Glu Thr Glu
                    50                      55                      60
Arg Ser Ala Leu Asp Val Lys Leu Lys His Ala Arg Asn Gln Val Asp
                    65                      70                      75                      80
Val Glu Ile Lys Arg Arg Gln Arg Ala Glu Ala Asp Cys Glu Lys Leu
                    85                      90                      95
Glu Arg Gln Ile Gln Leu Ile Arg Glu Met Leu Met Cys Asp Thr Ser
                    100                     105                     110
Gly Ser Ile Gln Leu Ser Glu Glu Gln Lys Ser Ala Leu Ala Phe Leu
                    115                     120                     125
Asn Arg Gly Gln Pro Ser Ser Ser Asn Ala Gly Asn Lys Arg Leu Ser
                    130                     135                     140
Thr Ile Asp Glu Ser Gly Ser Ile Leu Ser His Ile Ser Phe Asp Lys
                    145                     150                     155                     160
Thr Asp Glu Ser Leu Asp Trp Asp Ser Ser Leu Val Lys Thr Phe Lys

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144

				165					170					175	
Leu	Lys	Lys	Arg	Glu	Lys	Arg	Arg	Ser	Thr	Ser	Arg	Gln	Phe	Val	Asp
			180					185					190		
Gly	Pro	Pro	Gly	Pro	Val	Lys	Lys	Thr	Arg	Ser	Ile	Gly	Ser	Ala	Val
		195					200					205			
Asp	Gln	Gly	Asn	Glu	Ser	Ile	Val	Ala	Lys	Thr	Thr	Val	Thr	Val	Pro
	210					215					220				
Asn	Asp	Gly	Gly	Pro	Ile	Glu	Ala	Val	Ser	Thr	Ile	Glu	Thr	Val	Pro
225				230		230				235					240
Tyr	Trp	Thr	Arg	Ser	Arg	Arg	Lys	Thr	Gly	Thr	Leu	Gln	Pro	Trp	Asn
				245					250					255	
Ser	Asp	Ser	Thr	Leu	Asn	Ser	Arg	Gln	Leu	Glu	Pro	Arg	Thr	Glu	Thr
			260					265					270		
Asp	Ser	Val	Gly	Thr	Pro	Gln	Ser	Asn	Gly	Gly	Met	Arg	Leu	His	Asp
		275					280					285			
Phe	Val	Ser	Lys	Thr	Val	Ile	Lys	Pro	Glu	Ser	Cys	Val	Pro	Cys	Gly
	290					295					300				
Lys	Arg	Ile	Lys	Phe	Gly	Lys	Leu	Ser	Leu	Lys	Cys	Arg	Asp	Cys	Arg
305				310						315					320
Val	Val	Ser	His	Pro	Glu	Cys	Arg	Asp	Arg	Cys	Pro	Leu	Pro	Cys	Ile
				325					330					335	
Pro	Thr	Leu	Ile	Gly	Thr	Pro	Val	Lys	Ile	Gly	Glu	Gly	Met	Leu	Ala
			340					345					350		
Asp	Phe	Val	Ser	Gln	Thr	Ser	Pro	Met	Ile	Pro	Ser	Ile	Val	Val	His
		355					360					365			
Cys	Val	Asn	Glu	Ile	Glu	Gln	Arg	Gly	Leu	Thr	Glu	Thr	Gly	Leu	Tyr
	370					375					380				
Arg	Ile	Ser	Gly	Cys	Asp	Arg	Thr	Val	Lys	Glu	Leu	Lys	Glu	Lys	Phe
385				390						395					400
Leu	Arg	Val	Lys	Thr	Val	Pro	Leu	Leu	Ser	Lys	Val	Asp	Asp	Ile	His
				405				410						415	
Ala	Ile	Cys	Ser	Leu	Leu	Lys	Asp	Phe	Leu	Arg	Asn	Leu	Lys	Glu	Pro
			420					425					430		
Leu	Leu	Thr	Phe	Arg	Leu	Asn	Arg	Ala	Phe	Met	Glu	Ala	Ala	Glu	Ile
		435					440					445			
Thr	Asp	Glu	Asp	Asn	Ser	Ile	Ala	Ala	Met	Tyr	Gln	Ala	Val	Gly	Glu
	450					455					460				
Leu	Pro	Gln	Ala	Asn	Arg	Asp	Thr	Leu	Ala	Phe	Leu	Met	Ile	His	Leu
465				470						475					480
Gln	Arg	Val	Ala	Gln	Ser	Pro	His	Thr	Lys	Met	Asp	Val	Ala	Asn	Leu
				485					490					495	
Ala	Lys	Val	Phe	Gly	Pro	Thr	Ile	Val	Ala	His	Ala	Val	Pro	Asn	Pro
			500					505					510		
Asp	Pro	Val	Thr	Met	Leu	Gln	Asp	Ile	Lys	Arg	Gln	Pro	Lys	Val	Val
		515													

145

<210> 414
 <211> 3061
 <212> DNA
 <213> Homo sapiens

<400> 414
 cggcacgagg cgacttttggg ggaggtagtt ctttggcagc gggcatggcg ggtaccgtgg 60
 tgctggacga tgtggagctg cgggaggctc agagagatta cctggacttc ctggacgacg 120
 aggaagacca gggaatttat cagagcaaag ttcgggagct gatcagtgac aaccaatacc 180
 ggctgattgt caatgtgaat gacctgcgca ggaacaaacga gaagagggtc aaccggcttc 240
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146

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147

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<212> DNA

<213> Homo sapiens

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<211> 2910

<212> DNA

<213> Homo sapiens

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148

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<213> Homo sapiens

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149

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<212> DNA

<213> Homo sapiens

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152

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153

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154

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		515					520					525			
Met	Pro	Leu	Gly	Ser	Ala	Val	Asp	Ile	Leu	Ala	Thr	Asp	Asp	Pro	Asn
		530				535						540			
Phe	Ser	Gln	Glu	Asp	Gln	Gln	Asp	Thr	Gln	Ile	Tyr	Glu	Lys	His	Asp
545					550					555					560
Asn	Leu	Leu	His	Gly	Thr	Lys	Lys	Lys	Lys	Glu	Lys	Met	Val	Ser	Ala
			565						570						575
Ala	Phe	Met	Lys	Lys	Tyr	Ile	His	Val	Ala	Lys	Ile	Ile	Lys	Pro	Val
			580					585						590	
Leu	Thr	Gln	Glu	Ser	Ala	Thr	Tyr	Ile	Ala	Glu	Glu	Tyr	Ser	Arg	Leu
		595					600					605			
Arg	Ser	Gln	Asp	Ser	Met	Ser	Ser	Asp	Thr	Ala	Arg	Thr	Ser	Pro	Val
		610				615						620			
Thr	Ala	Arg	Thr	Leu	Glu	Thr	Leu	Ile	Arg	Leu	Ala	Thr	Ala	His	Ala
625					630					635					640
Lys	Ala	Arg	Met	Ser	Lys	Thr	Val	Asp	Leu	Gln	Asp	Ala	Glu	Glu	Ala
			645						650						655
Val	Glu	Leu	Val	Gln	Tyr	Ala	Tyr	Phe	Lys	Lys	Val	Leu	Glu	Lys	Glu
		660						665							670
Lys	Lys	Arg	Lys	Lys	Arg	Ser	Glu	Asp	Glu	Ser	Glu	Thr	Glu	Asp	Glu
		675					680					685			
Glu	Glu	Lys	Ser	Gln	Glu	Asp	Gln	Glu	Gln	Lys	Arg	Lys	Arg	Arg	Lys
		690				695					700				
Thr	Arg	Gln	Pro	Asp	Ala	Lys	Asp	Gly	Asp	Ser	Tyr	Asp	Pro	Tyr	Asp
705					710					715					720
Phe	Ser	Asp	Thr	Glu	Glu	Glu	Met	Pro	Gln	Val	His	Thr	Pro	Lys	Thr
				725					730						735

155

Ala Asp Ser Gln Glu Thr Lys Glu Ser Gln Lys Val Glu Leu Ser Glu
 740 745 750
 Ser Arg Leu Lys Ala Phe Lys Val Ala Leu Leu Asp Val Phe Arg Glu
 755 760 765
 Ala His Ala Gln Ser Ile Gly Met Asn Arg Leu Thr Glu Ser Ile Asn
 770 775 780
 Arg Asp Ser Glu Glu Pro Phe Ser Ser Val Glu Ile Gln Ala Ala Leu
 785 790 795 800
 Ser Lys Met Gln Asp Asp Asn Gln Val Met Val Ser Glu Gly Ile Ile
 805 810 815
 Phe Leu Ile

<210> 426
 <211> 178
 <212> PRT
 <213> Homo sapiens

<400> 426
 Glu Pro Arg Gly Ser Arg Ala Arg Phe Gly Cys Trp Arg Leu Gln Pro
 5 10 15
 Glu Phe Lys Pro Lys Gln Leu Glu Gly Thr Met Ala Asn Cys Glu Arg
 20 25 30
 Thr Phe Ile Ala Ile Lys Pro Asp Gly Val Gln Arg Gly Leu Val Gly
 35 40 45
 Glu Ile Ile Lys Arg Phe Glu Gln Lys Gly Phe Arg Leu Val Gly Leu
 50 55 60
 Lys Phe Met Gln Ala Ser Glu Asp Leu Leu Lys Glu His Tyr Val Asp
 65 70 75 80
 Leu Lys Asp Arg Pro Phe Phe Ala Gly Leu Val Lys Tyr Met His Ser
 85 90 95
 Gly Pro Val Val Ala Met Val Trp Glu Gly Leu Asn Val Val Lys Thr
 100 105 110
 Gly Arg Val Met Leu Gly Glu Thr Asn Pro Ala Asp Ser Lys Pro Gly
 115 120 125
 Thr Ile Arg Gly Asp Phe Cys Ile Gln Val Gly Arg Asn Ile Ile His
 130 135 140
 Gly Ser Asp Ser Val Glu Ser Ala Glu Lys Glu Ile Gly Leu Trp Phe
 145 150 155 160
 His Pro Glu Glu Leu Val Asp Tyr Thr Ser Cys Ala Gln Asn Trp Ile
 165 170 175
 Tyr Glu

<210> 427
 <211> 570
 <212> PRT
 <213> Homo sapiens

<400> 427
 Thr Glu Arg Ser Ala Leu Asp Val Lys Leu Lys His Ala Arg Asn Gln
 5 10 15
 Val Asp Val Glu Ile Lys Arg Arg Gln Arg Ala Glu Ala Asp Cys Glu
 20 25 30
 Lys Leu Glu Arg Gln Ile Gln Leu Ile Arg Glu Met Leu Met Cys Asp
 35 40 45
 Thr Ser Gly Ser Ile Gln Leu Ser Glu Glu Gln Lys Ser Ala Leu Ala
 50 55 60
 Phe Leu Asn Arg Gly Gln Pro Ser Ser Ser Asn Ala Gly Asn Lys Arg

156

65					70					75				80	
Leu	Ser	Thr	Ile	Asp	Glu	Ser	Gly	Ser	Ile	Leu	Ser	Asp	Ile	Ser	Phe
				85					90					95	
Asp	Lys	Thr	Asp	Glu	Ser	Leu	Asp	Trp	Asp	Ser	Ser	Leu	Val	Lys	Thr
			100					105					110		
Phe	Lys	Leu	Lys	Lys	Arg	Glu	Lys	Arg	Arg	Ser	Thr	Ser	Arg	Gln	Phe
		115					120					125			
Val	Asp	Gly	Pro	Pro	Gly	Pro	Val	Lys	Lys	Thr	Arg	Ser	Ile	Gly	Ser
		130				135					140				
Ala	Val	Asp	Gln	Gly	Asn	Glu	Ser	Ile	Val	Ala	Lys	Thr	Thr	Val	Thr
145					150					155					160
Val	Pro	Asn	Asp	Gly	Gly	Pro	Ile	Glu	Ala	Val	Ser	Thr	Ile	Glu	Thr
			165					170						175	
Val	Pro	Tyr	Trp	Thr	Arg	Ser	Arg	Arg	Lys	Thr	Gly	Thr	Leu	Gln	Pro
		180					185						190		
Trp	Asn	Ser	Asp	Ser	Thr	Leu	Asn	Ser	Arg	Gln	Leu	Glu	Pro	Arg	Thr
		195					200					205			
Glu	Thr	Asp	Ser	Val	Gly	Thr	Pro	Gln	Ser	Asn	Gly	Gly	Met	Arg	Leu
	210				215						220				
His	Asp	Phe	Val	Ser	Lys	Thr	Val	Ile	Lys	Pro	Glu	Ser	Cys	Val	Pro
225					230					235					240
Cys	Gly	Lys	Arg	Ile	Lys	Phe	Gly	Lys	Leu	Ser	Leu	Lys	Cys	Arg	Asp
			245						250					255	
Cys	Arg	Val	Val	Ser	His	Pro	Glu	Cys	Arg	Asp	Arg	Cys	Pro	Leu	Pro
		260						265					270		
Cys	Ile	Pro	Thr	Leu	Ile	Gly	Thr	Pro	Val	Lys	Ile	Gly	Glu	Gly	Met
	275					280						285			
Leu	Ala	Asp	Phe	Val	Ser	Gln	Thr	Ser	Pro	Met	Ile	Pro	Ser	Ile	Val
	290					295					300				
Val	His	Cys	Val	Asn	Glu	Ile	Glu	Gln	Arg	Gly	Leu	Thr	Glu	Thr	Gly
305					310					315					320
Leu	Tyr	Arg	Ile	Ser	Gly	Cys	Asp	Arg	Thr	Val	Lys	Glu	Leu	Lys	Glu
			325						330					335	
Lys	Phe	Leu	Arg	Val	Lys	Thr	Val	Pro	Leu	Leu	Ser	Lys	Val	Asp	Asp
			340					345					350		
Ile	His	Ala	Ile	Cys	Ser	Leu	Leu	Lys	Asp	Phe	Leu	Arg	Asn	Leu	Lys
	355					360						365			
Glu	Pro	Leu	Leu	Thr	Phe	Arg	Leu	Asn	Arg	Ala	Phe	Met	Glu	Ala	Ala
	370				375						380				
Glu	Ile	Thr	Asp	Glu	Asp	Asn	Ser	Ile	Ala	Ala	Met	Tyr	Gln	Ala	Val
385					390					395					400
Gly	Glu	Leu	Pro	Gln	Ala	Asn	Arg	Asp	Thr	Leu	Ala	Phe	Leu	Met	Ile
			405					410						415	
His	Leu	Gln	Arg	Val	Ala	Gln	Ser	Pro	His	Thr	Lys	Met	Asp	Val	Ala
		420						425					430		
Asn	Leu	Ala	Lys	Val	Phe	Gly	Pro	Thr	Ile	Val	Ala	His	Ala	Val	Pro
	435					440						445			
Asn	Pro	Asp	Pro	Val	Thr	Met	Leu	Gln	Asp	Ile	Lys	Arg	Gln	Pro	Lys
	450				455						460				
Val	Val	Glu	Arg	Leu	Leu	Ser	Leu	Pro	Leu	Glu	Tyr	Trp	Ser	Gln	Phe
465					470					475					480
Met	Met	Val	Glu	Gln	Glu	Asn	Ile	Asp	Pro	Leu	His	Val	Ile	Glu	Asn
			485					490						495	
Ser	Asn	Ala	Phe	Ser	Thr	Pro	Gln	Thr	Pro	Asp	Ile	Lys	Val	Ser	Leu
		500						505					510		
Leu	Gly	Pro	Val	Thr	Thr	Pro	Glu	His	Gln	Leu	Leu	Lys	Thr	Pro	Ser
		515					520						525		
Ser	Ser	Ser	Leu	Ser	Gln	Arg	Val	Arg	Ser	Thr	Leu	Thr	Lys	Asn	Thr
	530					535					540				

157

Pro Arg Phe Gly Ser Lys Ser Lys Ser Ala Thr Asn Leu Gly Arg Gln
 545 550 555 560
 Gly Asn Phe Phe Ala Ser Pro Met Leu Lys
 565 570

<210> 428
 <211> 532
 <212> PRT
 <213> Homo sapiens

<400> 428

Leu Leu Asp Ala Gly Pro Gln Phe Pro Ala Ile Gly Val Gly Ser Phe
 5 10 15
 Ala Arg His His His His Ser Ala Ala Ala Ala Ala Ala Ala Ala
 20 25 30
 Glu Met Gln Asp Arg Glu Leu Ser Leu Ala Ala Ala Gln Asn Gly Phe
 35 40 45
 Val Asp Ser Ala Ala Ala His Met Gly Ala Phe Lys Leu Asn Pro Gly
 50 55 60
 Ala His Glu Leu Ser Pro Gly Gln Ser Ser Ala Phe Thr Ser Gln Gly
 65 70 75 80
 Pro Gly Ala Tyr Pro Gly Ser Ala Ala Ala Ala Ala Ala Ala Ala
 85 90 95
 Leu Gly Pro His Ala Ala His Val Gly Ser Tyr Ser Gly Pro Pro Phe
 100 105 110
 Asn Ser Thr Arg Asp Phe Leu Phe Arg Ser Ala Arg Leu Pro Gly Thr
 115 120 125
 Ser Ala Pro Gly Gly Gly Gln His Gly Leu Phe Gly Pro Gly Ala Gly
 130 135 140
 Gly Leu His His Ala His Ser Asp Ala Gln Gly His Leu Leu Phe Pro
 145 150 155 160
 Gly Leu Pro Glu Gln His Gly Pro His Gly Ser Gln Asn Val Leu Asn
 165 170 175
 Gly Gln Met Arg Leu Gly Leu Pro Gly Glu Val Phe Gly Arg Ser Glu
 180 185 190
 Gln Tyr Arg Gln Val Ala Ser Pro Arg Thr Asp Pro Tyr Ser Ala Ala
 195 200 205
 Gln Leu His Asn Gln Tyr Gly Pro Met Asn Met Asn Met Gly Met Asn
 210 215 220
 Met Ala Ala Ala Ala Ala His His His His His His His His Pro
 225 230 235 240
 Gly Ala Phe Phe Arg Tyr Met Arg Gln Gln Cys Ile Lys Gln Glu Leu
 245 250 255
 Ile Cys Lys Trp Ile Asp Pro Glu Gln Leu Ser Asn Pro Lys Lys Ser
 260 265 270
 Cys Asn Lys Thr Phe Ser Thr Met His Glu Leu Val Thr His Val Ser
 275 280 285
 Val Glu His Val Gly Gly Pro Glu Gln Ser Asn His Val Cys Phe Trp
 290 295 300
 Glu Glu Cys Pro Arg Glu Gly Lys Pro Phe Lys Ala Lys Tyr Lys Leu
 305 310 315 320
 Val Asn His Ile Arg Val His Thr Gly Glu Lys Pro Phe Pro Cys Pro
 325 330 335
 Phe Pro Gly Cys Gly Lys Val Phe Ala Arg Ser Glu Asn Leu Lys Ile
 340 345 350
 His Lys Arg Thr His Thr Gly Glu Lys Pro Phe Gln Cys Glu Phe Glu
 355 360 365
 Gly Cys Asp Arg Arg Phe Ala Asn Ser Ser Asp Arg Lys Lys His Met
 370 375 380

158

His Val His Thr Ser Asp Lys Pro Tyr Leu Cys Lys Met Cys Asp Lys
 385 390 395 400
 Ser Tyr Thr His Pro Ser Ser Leu Arg Lys His Met Lys Val His Glu
 405 410 415
 Ser Ser Pro Gln Gly Ser Glu Ser Ser Pro Ala Ala Ser Ser Gly Tyr
 420 425 430
 Glu Ser Ser Thr Pro Pro Gly Leu Val Ser Pro Ser Ala Glu Pro Gln
 435 440 445
 Ser Ser Ser Asn Leu Ser Pro Ala Ala Ala Ala Ala Ala Ala Ala
 450 455 460
 Ala Ala Ala Ala Ala Val Ser Ala Val His Arg Gly Gly Gly Ser
 465 470 475 480
 Gly Ser Gly Gly Ala Gly Gly Gly Ser Gly Gly Ser Gly Ser Gly
 485 490 495
 Gly Gly Gly Gly Gly Ala Gly Gly Gly Gly Gly Gly Ser Ser Gly Gly
 500 505 510
 Gly Ser Gly Thr Ala Gly Gly His Ser Gly Leu Ser Ser Asn Phe Asn
 515 520 525
 Glu Trp Tyr Val
 530

<210> 429

<211> 629

<212> PRT

<213> Homo sapiens

<400> 429

Gly Gly Ala Pro Ala Ser Phe Pro Gly Arg Ala Pro Arg Ser Leu Ala
 5 10 15
 Ser Gln Pro Ala Ala Arg Ala Ala Ala Pro Ala Met Pro Ser Ala
 20 25 30
 Lys Gln Arg Gly Ser Lys Gly Gly His Gly Ala Ala Ser Pro Ser Glu
 35 40 45
 Lys Gly Ala His Pro Ser Gly Gly Ala Asp Asp Val Ala Lys Lys Pro
 50 55 60
 Pro Pro Ala Pro Gln Gln Pro Pro Pro Pro Ala Pro His Pro Gln
 65 70 75 80
 Gln His Pro Gln Gln His Pro Gln Asn Gln Ala His Gly Lys Gly Gly
 85 90 95
 His Arg Gly Gly Gly Gly Gly Gly Gly Lys Ser Ser Ser Ser Ser
 100 105 110
 Ala Ser Ala Ala Ala Ala Ala Ala Ala Ser Ser Ser Ala Ser Cys
 115 120 125
 Ser Arg Arg Leu Gly Arg Ala Leu Asn Phe Leu Phe Tyr Leu Ala Leu
 130 135 140
 Val Ala Ala Ala Ala Phe Ser Gly Trp Cys Val His His Val Leu Glu
 145 150 155 160
 Glu Val Gln Gln Val Arg Arg Ser His Gln Asp Phe Ser Arg Gln Arg
 165 170 175
 Glu Glu Leu Gly Gln Gly Leu Gln Gly Val Glu Gln Lys Val Gln Ser
 180 185 190
 Leu Gln Ala Thr Phe Gly Thr Phe Glu Ser Ile Leu Arg Ser Ser Gln
 195 200 205
 His Lys Gln Asp Leu Thr Glu Lys Ala Val Lys Gln Gly Glu Ser Glu
 210 215 220
 Val Ser Arg Ile Ser Glu Val Leu Gln Lys Leu Gln Asn Glu Ile Leu
 225 230 235 240
 Lys Asp Leu Ser Asp Gly Ile His Val Val Lys Asp Ala Arg Glu Arg

159

245 250 255
 Asp Phe Thr Ser Leu Glu Asn Thr Val Glu Glu Arg Leu Thr Glu Leu
 260 265 270
 Thr Lys Ser Ile Asn Asp Asn Ile Ala Ile Phe Thr Glu Val Gln Lys
 275 280 285
 Arg Ser Gln Lys Glu Ile Asn Asp Met Lys Ala Lys Val Ala Ser Leu
 290 295 300
 Glu Glu Ser Glu Gly Asn Lys Gln Asp Leu Lys Ala Leu Lys Glu Ala
 305 310 315 320
 Val Lys Glu Ile Gln Thr Ser Ala Lys Ser Arg Glu Trp Asp Met Glu
 325 330 335
 Ala Leu Arg Ser Thr Leu Gln Thr Met Glu Ser Asp Ile Tyr Thr Glu
 340 345 350
 Val Arg Glu Leu Val Ser Leu Lys Gln Glu Gln Gln Ala Phe Lys Glu
 355 360 365
 Ala Ala Asp Thr Glu Arg Leu Ala Leu Gln Ala Leu Thr Glu Lys Leu
 370 375 380
 Leu Arg Ser Glu Glu Ser Val Ser Arg Leu Pro Glu Glu Ile Arg Arg
 385 390 395 400
 Leu Glu Glu Glu Leu Arg Gln Leu Lys Ser Asp Ser His Gly Pro Lys
 405 410 415
 Glu Asp Gly Gly Phe Arg His Ser Glu Ala Phe Glu Ala Leu Gln Gln
 420 425 430
 Lys Ser Gln Gly Leu Asp Ser Arg Leu Gln His Val Glu Asp Gly Val
 435 440 445
 Leu Ser Met Gln Val Ala Ser Ala Arg Gln Thr Glu Ser Leu Glu Ser
 450 455 460
 Leu Leu Ser Lys Ser Gln Glu His Glu Gln Arg Leu Ala Pro Ala Gly
 465 470 475 480
 Ala Leu Glu Gly Leu Gly Ser Ser Glu Ala Asp Gln Asp Gly Leu Ala
 485 490 495
 Ser Thr Val Arg Ser Leu Gly Glu Thr Gln Leu Val Leu Tyr Gly Asp
 500 505 510
 Val Glu Glu Leu Lys Arg Ser Val Gly Glu Leu Pro Ser Thr Val Glu
 515 520 525
 Ser Leu Gln Lys Val Gln Glu Gln Val His Thr Leu Leu Ser Gln Asp
 530 535 540
 Gln Ala Gln Ala Ala Arg Leu Pro Pro Gln Asp Phe Leu Asp Arg Leu
 545 550 555 560
 Ser Ser Leu Asp Asn Leu Lys Ala Ser Val Ser Gln Val Glu Ala Asp
 565 570 575
 Leu Lys Met Leu Arg Thr Ala Val Asp Ser Leu Val Ala Tyr Ser Val
 580 585 590
 Lys Ile Glu Thr Asn Glu Asn Asn Leu Glu Ser Ala Lys Gly Leu Leu
 595 600 605
 Asp Asp Leu Arg Asn Asp Leu Asp Arg Leu Phe Val Lys Val Glu Lys
 610 615 620
 Ile His Glu Lys Val
 625

<210> 430

<211> 147

<212> PRT

<213> Homo sapiens

<400> 430

Pro Gln Trp Cys Pro Arg Ser Gln Ala Arg Ser Ser Ala Ala Ala Ala
 5 10 15

160

Ala Arg Ala Ser Val Pro Leu Arg Gly Ser Pro Gly Pro Ser Ala Ile
 20 25 30
 Met Pro Met Phe Ile Val Asn Thr Asn Val Pro Arg Ala Ser Val Pro
 35 40 45
 Asp Gly Phe Leu Ser Glu Leu Thr Gln Gln Leu Ala Gln Ala Thr Gly
 50 55 60
 Lys Pro Pro Gln Tyr Ile Ala Val His Val Val Pro Asp Gln Leu Met
 65 70 75 80
 Ala Phe Gly Gly Ser Ser Glu Pro Cys Ala Leu Cys Ser Leu His Ser
 85 90 95
 Ile Gly Lys Ile Gly Gly Ala Gln Asn Arg Ser Tyr Ser Lys Leu Leu
 100 105 110
 Cys Gly Leu Leu Ala Glu Arg Leu Arg Ile Ser Pro Asp Arg Val Tyr
 115 120 125
 Ile Asn Tyr Tyr Asp Met Asn Ala Ala Asn Val Gly Trp Asn Asn Ser
 130 135 140
 Thr Phe Ala
 145

<210> 431

<211> 775

<212> PRT

<213> Homo sapiens

<400> 431

Leu Ala Pro Pro Arg Gln Leu Glu Ser Thr Ser Ser Ala Val Arg Leu
 5 10 15
 Thr Glu Met Leu Arg Ala Cys Gln Leu Ser Gly Val Thr Ala Ala Ala
 20 25 30
 Gln Ser Cys Leu Cys Gly Lys Phe Val Leu Arg Pro Leu Arg Pro Cys
 35 40 45
 Arg Arg Tyr Ser Thr Ser Gly Ser Ser Gly Leu Thr Thr Gly Lys Ile
 50 55 60
 Ala Gly Ala Gly Leu Leu Phe Val Gly Gly Gly Ile Gly Gly Thr Ile
 65 70 75 80
 Leu Tyr Ala Lys Trp Asp Ser His Phe Arg Glu Ser Val Glu Lys Thr
 85 90 95
 Ile Pro Tyr Ser Asp Lys Leu Phe Glu Met Val Leu Gly Pro Ala Ala
 100 105 110
 Tyr Asn Val Pro Leu Pro Lys Lys Ser Ile Gln Ser Gly Pro Leu Lys
 115 120 125
 Ile Ser Ser Val Ser Glu Val Met Lys Glu Ser Lys Gln Pro Ala Ser
 130 135 140
 Gln Leu Gln Lys Gln Lys Gly Asp Thr Pro Ala Ser Ala Thr Ala Pro
 145 150 155 160
 Thr Glu Ala Ala Gln Ile Ile Ser Ala Ala Gly Asp Thr Leu Ser Val
 165 170 175
 Pro Ala Pro Ala Val Gln Pro Glu Glu Ser Leu Lys Thr Asp His Pro
 180 185 190
 Glu Ile Gly Glu Gly Lys Pro Thr Pro Ala Leu Ser Glu Glu Ala Ser
 195 200 205
 Ser Ser Ser Ile Arg Glu Arg Pro Pro Glu Glu Val Ala Ala Arg Leu
 210 215 220
 Ala Gln Gln Glu Lys Gln Glu Gln Val Lys Ile Glu Ser Leu Ala Lys
 225 230 235 240
 Ser Leu Glu Asp Ala Leu Arg Gln Thr Ala Ser Val Thr Leu Gln Ala
 245 250 255
 Ile Ala Ala Gln Asn Ala Ala Val Gln Ala Val Asn Ala His Ser Asn

161

		260						265				270			
Ile	Leu	Lys	Ala	Ala	Met	Asp	Asn	Ser	Glu	Ile	Ala	Gly	Glu	Lys	Lys
		275						280				285			
Ser	Ala	Gln	Trp	Arg	Thr	Val	Glu	Gly	Ala	Leu	Lys	Glu	Arg	Arg	Lys
		290						295				300			
Ala	Val	Asp	Glu	Ala	Ala	Asp	Ala	Leu	Leu	Lys	Ala	Lys	Glu	Glu	Leu
305					310					315					320
Glu	Lys	Met	Lys	Ser	Val	Ile	Glu	Asn	Ala	Lys	Lys	Lys	Glu	Val	Ala
				325					330					335	
Gly	Ala	Lys	Pro	His	Ile	Thr	Ala	Ala	Glu	Gly	Lys	Leu	His	Asn	Met
		340						345					350		
Ile	Val	Asp	Leu	Asp	Asn	Val	Val	Lys	Lys	Val	Gln	Ala	Ala	Gln	Ser
		355					360					365			
Glu	Ala	Lys	Val	Val	Ser	Gln	Tyr	His	Glu	Leu	Val	Val	Gln	Ala	Arg
370						375					380				
Asp	Asp	Phe	Lys	Arg	Glu	Leu	Asp	Ser	Ile	Thr	Pro	Glu	Val	Leu	Pro
385					390				395						400
Gly	Trp	Lys	Gly	Met	Ser	Val	Ser	Asp	Leu	Ala	Asp	Lys	Leu	Ser	Thr
				405				410						415	
Asp	Asp	Leu	Asn	Ser	Leu	Ile	Ala	His	Ala	His	Arg	Arg	Ile	Asp	Gln
		420					425						430		
Leu	Asn	Arg	Glu	Leu	Ala	Glu	Gln	Lys	Ala	Thr	Glu	Lys	Gln	His	Ile
435						440						445			
Thr	Leu	Ala	Leu	Glu	Lys	Gln	Lys	Leu	Glu	Glu	Lys	Arg	Ala	Phe	Asp
450						455					460				
Ser	Ala	Val	Ala	Lys	Ala	Leu	Glu	His	His	Arg	Ser	Glu	Ile	Gln	Ala
465					470				475						480
Glu	Gln	Asp	Arg	Lys	Ile	Glu	Glu	Val	Arg	Asp	Ala	Met	Glu	Asn	Glu
				485				490						495	
Met	Arg	Thr	Gln	Leu	Arg	Arg	Gln	Ala	Ala	His	Thr	Asp	His	Leu	
		500					505					510			
Arg	Asp	Val	Leu	Arg	Val	Gln	Glu	Gln	Glu	Leu	Lys	Ser	Glu	Phe	Glu
		515				520						525			
Gln	Asn	Leu	Ser	Glu	Lys	Leu	Ser	Glu	Gln	Glu	Leu	Gln	Phe	Arg	Arg
530						535					540				
Leu	Ser	Gln	Glu	Gln	Val	Asp	Asn	Phe	Thr	Leu	Asp	Ile	Asn	Thr	Ala
545					550					555					560
Tyr	Ala	Arg	Leu	Arg	Gly	Ile	Glu	Gln	Ala	Val	Gln	Ser	His	Ala	Val
				565					570					575	
Ala	Glu	Glu	Glu	Ala	Arg	Lys	Ala	His	Gln	Leu	Trp	Leu	Ser	Val	Glu
				580			585					590			
Ala	Leu	Lys	Tyr	Ser	Met	Lys	Thr	Ser	Ser	Ala	Glu	Thr	Pro	Thr	Ile
		595				600					605				
Pro	Leu	Gly	Ser	Ala	Val	Glu	Ala	Ile	Lys	Ala	Asn	Cys	Ser	Asp	Asn
610						615				620					
Glu	Phe	Thr	Gln	Ala	Leu	Thr	Ala	Ala	Ile	Pro	Pro	Glu	Ser	Leu	Thr
625					630					635					640
Arg	Gly	Val	Tyr	Ser	Glu	Glu	Thr	Leu	Arg	Ala	Arg	Phe	Tyr	Ala	Val
				645					650					655	
Gln	Lys	Leu	Ala	Arg	Arg	Val	Ala	Met	Ile	Asp	Glu	Thr	Arg	Asn	Ser
				660			665						670		
Leu	Tyr	Gln	Tyr	Phe	Leu	Ser	Tyr	Leu	Gln	Ser	Leu	Leu	Leu	Phe	Pro
		675					680				685				
Pro	Gln	Gln	Leu	Lys	Pro	Pro	Pro	Glu	Leu	Cys	Pro	Glu	Asp	Ile	Asn
690					695						700				
Thr	Phe	Lys	Leu	Leu	Ser	Tyr	Ala	Ser	Tyr	Cys	Ile	Glu	His	Gly	Asp
705					710					715					720
Leu	Glu	Leu	Ala	Ala	Lys	Phe	Val	Asn	Gln	Leu	Lys	Gly	Glu	Ser	Arg
				725					730						735

162

Arg Val Ala Gln Asp Trp Leu Lys Glu Ala Arg Met Thr Leu Glu Thr
 740 745 750
 Lys Gln Ile Val Glu Ile Leu Thr Ala Tyr Ala Ser Ala Val Gly Ile
 755 760 765
 Gly Thr Thr Gln Val Gln Pro
 770 775

<210> 432
 <211> 741
 <212> PRT
 <213> Homo sapiens

<400> 432
 Arg Pro Lys Arg Leu Arg Thr Gly Asn Met Val Arg Ser Gly Asn Lys
 5 10 15
 Ala Ala Val Val Leu Cys Met Asp Val Gly Phe Thr Met Ser Asn Ser
 20 25 30
 Ile Pro Gly Ile Glu Ser Pro Phe Glu Gln Ala Lys Lys Val Ile Thr
 35 40 45
 Met Phe Val Gln Arg Gln Val Phe Ala Glu Asn Lys Asp Glu Ile Ala
 50 55 60
 Leu Val Leu Phe Gly Thr Asp Gly Thr Asp Asn Pro Leu Ser Gly Gly
 65 70 75 80
 Asp Gln Tyr Gln Asn Ile Thr Val His Arg His Leu Met Leu Pro Asp
 85 90 95
 Phe Asp Leu Leu Glu Asp Ile Glu Ser Lys Ile Gln Pro Gly Ser Gln
 100 105 110
 Gln Ala Asp Phe Leu Asp Ala Leu Ile Val Ser Met Asp Val Ile Gln
 115 120 125
 His Glu Thr Ile Gly Lys Lys Phe Glu Lys Arg His Ile Glu Ile Phe
 130 135 140
 Thr Asp Leu Ser Ser Arg Phe Ser Lys Ser Gln Leu Asp Ile Ile Ile
 145 150 155 160
 His Ser Leu Lys Lys Cys Asp Ile Ser Leu Gln Phe Phe Leu Pro Phe
 165 170 175
 Ser Leu Gly Lys Glu Asp Gly Ser Gly Asp Arg Gly Asp Gly Pro Phe
 180 185 190
 Arg Leu Gly Gly His Gly Pro Ser Phe Pro Leu Lys Gly Ile Thr Glu
 195 200 205
 Gln Gln Lys Glu Gly Leu Glu Ile Val Lys Met Val Met Ile Ser Leu
 210 215 220
 Glu Gly Glu Asp Gly Leu Asp Glu Ile Tyr Ser Phe Ser Glu Ser Leu
 225 230 235 240
 Arg Lys Leu Cys Val Phe Lys Lys Ile Glu Arg His Ser Ile His Trp
 245 250 255
 Pro Cys Arg Leu Thr Ile Gly Ser Asn Leu Ser Ile Arg Ile Ala Ala
 260 265 270
 Tyr Lys Ser Ile Leu Gln Glu Arg Val Lys Lys Thr Trp Thr Val Val
 275 280 285
 Asp Ala Lys Thr Leu Lys Lys Glu Asp Ile Gln Lys Glu Thr Val Tyr
 290 295 300
 Cys Leu Asn Asp Asp Asp Glu Thr Glu Val Leu Lys Glu Asp Ile Ile
 305 310 315 320
 Gln Gly Phe Arg Tyr Gly Ser Asp Ile Val Pro Phe Ser Lys Val Asp
 325 330 335
 Glu Glu Gln Met Lys Tyr Lys Ser Glu Gly Lys Cys Phe Ser Val Leu
 340 345 350
 Gly Phe Cys Lys Ser Ser Gln Val Gln Arg Arg Phe Phe Met Gly Asn

163

355	360	365
Gln Val Leu Lys Val Phe	Ala Ala Arg Asp Asp	Glu Ala Ala Ala Val
370	375	380
Ala Leu Ser Ser Leu Ile	His Ala Leu Asp Asp	Leu Asp Met Val Ala
385	390	395
Ile Val Arg Tyr Ala Tyr	Asp Lys Arg Ala Asn	Pro Gln Val Gly Val
405	410	415
Ala Phe Pro His Ile Lys	His Asn Tyr Glu Cys	Leu Val Tyr Val Gln
420	425	430
Leu Pro Phe Met Glu Asp	Leu Arg Gln Tyr Met	Phe Ser Ser Leu Lys
435	440	445
Asn Ser Lys Lys Tyr Ala	Pro Thr Glu Ala Gln	Leu Asn Ala Val Asp
450	455	460
Ala Leu Ile Asp Ser Met	Ser Leu Ala Lys Lys	Asp Glu Lys Thr Asp
465	470	475
Thr Leu Glu Asp Leu Phe	Pro Thr Thr Lys Ile	Pro Asn Pro Arg Phe
485	490	495
Gln Arg Leu Phe Gln Cys	Leu Leu His Arg Ala	Leu His Pro Arg Glu
500	505	510
Pro Leu Pro Pro Ile Gln	Gln His Ile Trp Asn	Met Leu Asn Pro Pro
515	520	525
Ala Glu Val Thr Thr Lys	Ser Gln Ile Pro Leu	Ser Lys Ile Lys Thr
530	535	540
Leu Phe Pro Leu Ile Glu	Ala Lys Lys Lys Asp	Gln Val Thr Ala Gln
545	550	555
Glu Ile Phe Gln Asp Asn	His Glu Asp Gly Pro	Thr Ala Lys Lys Leu
565	570	575
Lys Thr Glu Gln Gly Gly	Ala His Phe Ser Val	Ser Ser Leu Ala Glu
580	585	590
Gly Ser Val Thr Ser Val	Gly Ser Val Asn Pro	Ala Glu Asn Phe Arg
595	600	605
Val Leu Val Lys Gln Lys	Lys Ala Ser Phe Glu	Glu Ala Ser Asn Gln
610	615	620
Leu Ile Asn His Ile Glu	Gln Phe Leu Asp Thr	Asn Glu Thr Pro Tyr
625	630	635
Phe Met Lys Ser Ile Asp	Cys Ile Arg Ala Phe	Arg Glu Glu Ala Ile
645	650	655
Lys Phe Ser Glu Glu Gln	Arg Phe Asn Asn Phe	Leu Lys Ala Leu Gln
660	665	670
Glu Lys Val Glu Ile Lys	Gln Leu Asn His Phe	Trp Glu Ile Val Val
675	680	685
Gln Asp Gly Ile Thr Leu	Ile Thr Lys Glu Glu	Ala Ser Gly Ser Ser
690	695	700
Val Thr Ala Glu Glu Ala	Lys Lys Phe Leu Ala	Pro Lys Asp Lys Pro
705	710	715
Ser Gly Asp Thr Ala Ala	Val Phe Glu Glu Gly	Asp Val Asp Asp
725	730	735
Leu Leu Asp Met Ile		
740		

<210> 433

<211> 291

<212> PRT

<213> Homo sapiens

<400> 433

Phe Arg Pro Arg Tyr Glu Gly Arg Gly Arg Gly Cys Cys Gly Arg Val
5 10 15

164

Leu Leu Leu Arg Arg Gly Leu His Val Asp Cys Gly Lys Leu Gly Asn
 20 25 30
 Lys Leu Thr Ser Ser Cys Gly Lys Pro Ser Ser Asn Arg Met Ser Leu
 35 40 45
 Gln Trp Thr Ala Val Ala Thr Phe Leu Tyr Ala Glu Val Phe Val Val
 50 55 60
 Leu Leu Leu Cys Ile Pro Phe Ile Ser Pro Lys Arg Trp Gln Lys Ile
 65 70 75 80
 Phe Lys Ser Arg Leu Val Glu Leu Leu Val Ser Tyr Gly Asn Thr Phe
 85 90 95
 Phe Val Val Leu Ile Val Ile Leu Val Leu Val Ile Asp Ala Val
 100 105 110
 Arg Glu Ile Arg Lys Tyr Asp Asp Val Thr Glu Lys Val Asn Leu Gln
 115 120 125
 Asn Asn Pro Gly Ala Met Glu His Phe His Met Lys Leu Phe Arg Ala
 130 135 140
 Gln Arg Asn Leu Tyr Ile Ala Gly Phe Ser Leu Leu Leu Ser Phe Leu
 145 150 155 160
 Leu Arg Arg Leu Val Thr Leu Ile Ser Gln Gln Ala Thr Leu Leu Ala
 165 170 175
 Ser Asn Glu Ala Phe Lys Lys Gln Ala Glu Ser Ala Ser Glu Ala Ala
 180 185 190
 Lys Lys Tyr Met Glu Glu Asn Asp Gln Leu Lys Lys Gly Ala Ala Val
 195 200 205
 Asp Gly Gly Lys Leu Asp Val Gly Asn Ala Glu Val Lys Leu Glu Glu
 210 215 220
 Glu Asn Arg Ser Leu Lys Ala Asp Leu Gln Lys Leu Lys Asp Glu Leu
 225 230 235 240
 Ala Ser Thr Lys Gln Lys Leu Glu Lys Ala Glu Asn Gln Val Leu Ala
 245 250 255
 Met Arg Lys Gln Ser Glu Gly Leu Thr Lys Glu Tyr Asp Arg Leu Leu
 260 265 270
 Glu Glu His Ala Lys Leu Gln Ala Ala Val Asp Gly Pro Met Asp Lys
 275 280 285
 Lys Glu Glu
 290

<210> 434

<211> 349

<212> PRT

<213> Homo sapiens

<400> 434

Gly Val Ala Pro Trp Gly Arg Gly Arg Ala Ala Pro Arg Cys Ala Ser
 5 10 15
 Ala Thr Val Gly Gly Ser Gly Ile Gly Arg Leu Arg Gly Ile Thr Ser
 20 25 30
 Ser Gly Leu Lys Met Asp Asn Lys Lys Arg Leu Ala Tyr Ala Ile Ile
 35 40 45
 Gln Phe Leu His Asp Gln Leu Arg His Gly Gly Leu Ser Ser Asp Ala
 50 55 60
 Gln Glu Ser Leu Glu Val Ala Ile Gln Cys Leu Glu Thr Ala Phe Gly
 65 70 75 80
 Val Thr Val Glu Asp Ser Asp Leu Ala Leu Pro Gln Thr Leu Pro Glu
 85 90 95
 Ile Phe Glu Ala Ala Ala Thr Gly Lys Glu Met Pro Gln Asp Leu Arg
 100 105 110
 Ser Pro Ala Arg Thr Pro Pro Ser Glu Glu Asp Ser Ala Glu Ala Glu

165

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      115      120      125
Arg Leu Lys Thr Glu Gly Asn Glu Gln Met Lys Val Glu Asn Phe Glu
 130      135      140
Ala Ala Val His Phe Tyr Gly Lys Ala Ile Glu Leu Asn Pro Ala Asn
 145      150      155
Ala Val Tyr Phe Cys Asn Arg Ala Ala Ala Tyr Ser Lys Leu Gly Asn
      165      170      175
Tyr Ala Gly Ala Val Gln Asp Cys Glu Arg Ala Ile Cys Ile Asp Pro
      180      185      190
Ala Tyr Ser Lys Ala Tyr Gly Arg Met Gly Leu Ala Leu Ser Ser Leu
      195      200      205
Asn Lys His Val Glu Ala Val Ala Tyr Tyr Lys Lys Ala Leu Glu Leu
 210      215      220
Asp Pro Asp Asn Glu Thr Tyr Lys Ser Asn Leu Lys Ile Ala Glu Leu
 225      230      235
Lys Leu Arg Glu Ala Pro Ser Pro Thr Gly Gly Val Gly Ser Phe Asp
      245      250      255
Ile Ala Gly Leu Leu Asn Asn Pro Gly Phe Met Ser Met Ala Ser Asn
      260      265      270
Leu Met Asn Asn Pro Gln Ile Gln Gln Leu Met Ser Gly Met Ile Ser
      275      280      285
Gly Gly Asn Asn Pro Leu Gly Thr Pro Gly Thr Ser Pro Ser Gln Asn
 290      295      300
Asp Leu Ala Ser Leu Ile Gln Ala Gly Gln Gln Phe Ala Gln Gln Met
 305      310      315
Gln Gln Gln Asn Pro Glu Leu Ile Glu Gln Leu Arg Ser Gln Ile Arg
      325      330      335
Ser Arg Thr Pro Ser Ala Ser Asn Asp Asp Gln Gln Glu
      340      345

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<210> 435

<211> 519

<212> PRT

<213> Homo sapiens

<400> 435

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Gln Pro Ser Ala Glu Pro Arg Arg Thr Met Pro Ala Val Asp Lys Leu
      5      10      15
Leu Leu Glu Glu Ala Leu Gln Asp Ser Pro Gln Thr Arg Ser Leu Leu
      20      25      30
Ser Val Phe Glu Glu Asp Ala Gly Thr Leu Thr Asp Tyr Thr Asn Gln
      35      40      45
Leu Leu Gln Ala Met Gln Arg Val Tyr Gly Ala Gln Asn Glu Met Cys
      50      55      60
Leu Ala Thr Gln Gln Leu Ser Lys Gln Leu Leu Ala Tyr Glu Lys Gln
      65      70      75      80
Asn Phe Ala Leu Gly Lys Gly Asp Glu Glu Val Ile Ser Thr Leu His
      85      90      95
Tyr Phe Ser Lys Val Val Asp Glu Leu Asn Leu Leu His Thr Glu Leu
      100      105      110
Ala Lys Gln Leu Ala Asp Thr Met Val Leu Pro Ile Ile Gln Phe Arg
      115      120      125
Glu Lys Asp Leu Thr Glu Val Ser Thr Leu Lys Asp Leu Phe Gly Leu
      130      135      140
Ala Ser Asn Glu His Asp Leu Ser Met Ala Lys Tyr Ser Arg Leu Pro
 145      150      155
Lys Lys Lys Glu Asn Glu Lys Val Lys Thr Glu Val Gly Lys Glu Val
      165      170      175

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166

Ala Ala Ala Arg Arg Lys Gln His Leu Ser Ser Leu Gln Tyr Tyr Cys
 180 185 190
 Ala Leu Asn Ala Leu Gln Tyr Arg Lys Gln Met Ala Met Met Glu Pro
 195 200 205
 Met Ile Gly Phe Ala His Gly Gln Ile Asn Phe Phe Lys Lys Gly Ala
 210 215 220
 Glu Met Phe Ser Lys Arg Met Asp Ser Phe Leu Ser Ser Val Ala Asp
 225 230 235 240
 Met Val Gln Ser Ile Gln Val Glu Leu Glu Ala Glu Ala Glu Lys Met
 245 250 255
 Arg Val Ser Gln Gln Glu Leu Leu Ser Val Asp Glu Ser Val Tyr Thr
 260 265 270
 Pro Asp Ser Asp Val Ala Ala Pro Gln Ile Asn Arg Asn Leu Ile Gln
 275 280 285
 Lys Ala Gly Tyr Leu Asn Leu Arg Asn Lys Thr Gly Leu Val Thr Thr
 290 295 300
 Thr Trp Glu Arg Leu Tyr Phe Phe Thr Gln Gly Gly Asn Leu Met Cys
 305 310 315 320
 Gln Pro Arg Gly Ala Val Ala Gly Gly Leu Ile Gln Asp Leu Asp Asn
 325 330 335
 Cys Ser Val Met Ala Val Asp Cys Glu Asp Arg Arg Tyr Cys Phe Gln
 340 345 350
 Ile Thr Thr Pro Asn Gly Lys Ser Gly Ile Ile Leu Gln Ala Glu Ser
 355 360 365
 Arg Lys Glu Asn Glu Glu Trp Ile Cys Ala Ile Asn Asn Thr Ser Arg
 370 375 380
 Gln Ile Tyr Leu Thr Asp Asn Pro Glu Ala Val Ala Ile Lys Leu Asn
 385 390 395 400
 Gln Thr Ala Leu Gln Ala Val Thr Pro Ile Thr Ser Phe Gly Lys Lys
 405 410 415
 Gln Glu Ser Ser Cys Pro Ser Gln Asn Leu Lys Asn Ser Glu Met Glu
 420 425 430
 Asn Glu Asn Asp Lys Ile Val Pro Lys Ala Thr Ala Ser Leu Pro Glu
 435 440 445
 Ala Glu Glu Leu Ile Ala Pro Gly Thr Pro Ile Gln Phe Asp Ile Val
 450 455 460
 Leu Pro Ala Thr Glu Phe Leu Asp Gln Asn Arg Gly Ser Arg Arg Thr
 465 470 475 480
 Asn Pro Phe Gly Glu Thr Glu Asp Glu Ser Phe Pro Glu Ala Glu Asp
 485 490 495
 Ser Leu Leu Gln Gln Met Phe Ile Val Arg Phe Leu Gly Ser Met Ala
 500 505 510
 Val Lys Thr Asp Ser Thr Thr
 515

<210> 436

<211> 357

<212> PRT

<213> Homo sapiens

<400> 436

Met Leu Gln Ile His Leu Pro Gly Arg His Thr Leu Phe Val Arg Ala
 5 10 15
 Met Ile Asp Ser Gly Ala Ser Gly Asn Phe Ile Asp His Glu Tyr Val
 20 25 30
 Ala Gln Asn Gly Ile Pro Leu Arg Ile Lys Asp Trp Pro Ile Leu Val
 35 40 45
 Glu Ala Ile Asp Gly Arg Pro Ile Ala Ser Gly Pro Val Val His Glu

167

50	55	60
Thr His Asp Leu Ile Val Asp Leu Gly Asp His Arg Glu Val Leu Ser		
65	70	75
Phe Asp Val Thr Gln Ser Pro Phe Phe Pro Val Val Leu Gly Val Arg		
	85	90
Trp Leu Ser Thr His Asp Pro Asn Ile Thr Trp Ser Thr Arg Ser Ile		
	100	105
Val Phe Asp Ser Glu Tyr Cys Arg Tyr His Cys Arg Met Tyr Ser Pro		
	115	120
Ile Pro Pro Ser Leu Pro Pro Ala Pro Gln Pro Pro Leu Tyr Tyr		
	130	135
Pro Val Asp Gly Tyr Arg Val Tyr Gln Pro Val Arg Tyr Tyr Tyr Val		
145	150	155
Gln Asn Val Tyr Thr Pro Val Asp Glu His Val Tyr Pro Asp His Arg		
	165	170
Leu Val Asp Pro His Ile Glu Met Ile Pro Gly Ala His Ser Ile Pro		
	180	185
Ser Gly His Val Tyr Ser Leu Ser Glu Pro Glu Met Ala Ala Leu Arg		
	195	200
Asp Phe Val Ala Arg Asn Val Lys Asp Gly Leu Ile Thr Pro Thr Ile		
210	215	220
Ala Pro Asn Gly Ala Gln Val Leu Gln Val Lys Arg Gly Trp Lys Leu		
225	230	235
Gln Val Ser Tyr Asp Cys Arg Ala Pro Asn Asn Phe Thr Ile Gln Asn		
	245	250
Gln Tyr Pro Arg Leu Ser Ile Pro Asn Leu Glu Asp Gln Ala His Leu		
	260	265
Ala Thr Tyr Thr Glu Phe Val Pro Gln Ile Pro Gly Tyr Gln Thr Tyr		
	275	280
Pro Thr Tyr Ala Ala Tyr Pro Thr Tyr Pro Val Gly Phe Ala Trp Tyr		
	295	300
Pro Val Gly Arg Asp Gly Gln Gly Arg Ser Leu Tyr Val Pro Val Met		
305	310	315
Ile Thr Trp Asn Pro His Trp Tyr Arg Gln Pro Pro Val Pro Gln Tyr		
	325	330
Pro Pro Pro Gln Pro Pro Pro Pro Pro Pro Pro Pro Pro Pro Pro		
	340	345
Ser Tyr Ser Thr Leu		350
355		

<210> 437

<211> 501

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> (1)...(501)

<223> n = A,T,C or G

<400> 437

cgcaccagct ctctgctctc ccagcgcagc gccgccgccc ggccccctcca gcttcccggg	60
ccatggccaa cctggagcgc accttcacgc ccatcaagcc ggacggcgctg cagcgcggcc	120
tggtggggcga gatcatcaag cgcttcgagc agaagggtt ccgcctcgtg gccatgaagt	180
tcctccgggc ctctgaagaa cacctgaagc agcactacat tgacctgaaa gaccgaccat	240
tcttccctgg gctgggtgaag tacatgaact cagggccggt tgtggccatg gtctgggagg	300
ggctgaacgt ggtgaagaca ggccgagtga tgcttgggga gaccaatcca gcagattcaa	360

168

agccaggcac	cattcgtggg	gacttctgca	ttcaggttgg	caggaacatc	attcatggca	420
gtgattcagt	aaaaagtgt	gaaaaagaaa	tcancctatg	gtttaagcct	gaanaactgg	480
ttgactacaa	gtctttgtgt	c				501

<210> 438
 <211> 501
 <212> DNA
 <213> Homo sapiens

<400> 438						
tgaataactg	gagctgttgt	agaagaaaaa	cttctgattt	taatacattc	ttagcccaag	60
agggctgtac	aaaaggga	cacatgtgga	ctaaaaaaga	tgctgggaaa	aaagtgtgtc	120
catgtagaca	tgactggcat	cagactggag	ggtgaaagt	ccatttcagt	atatgctaaa	180
aactcacttc	cagaacttag	ccgagtagaa	gcaaatagca	cattgtttaa	tgtgcatatt	240
gtatttgaag	gagagaagga	atttgatcaa	aatgtgaaat	tatgggggtg	gattgatgta	300
aagcgaagt	atgtaactat	gactgcaaca	aagattgaaa	tcactatgag	aaaagctgaa	360
ccgatgcagt	gggcaagcct	tgaactgcct	gcagctaaaa	agcaggaaaa	acaaaaagat	420
gacacaacag	attgagtggg	agatggaagg	aaggctatta	cattatttcc	gaatttttaa	480
tactgtgtga	agtgggtggc	t				501

<210> 439
 <211> 501
 <212> DNA
 <213> Homo sapiens

<400> 439						
taaaacaagc	acttgataaa	cttaaaactgt	catcagggaa	tgaagaaaat	aagaaagaag	60
aagacaatga	tgaaattaag	attgggacct	catgtaagaa	tgagggggtg	tcaaagacat	120
accagggctc	agagagtcta	gaagaagtct	gtgtatatca	ttctggagta	cctattttcc	180
atgaggggat	gaaatactgg	agctgttgta	gaagaaaaac	ttctgatttt	aatacattct	240
tagcccaaga	gggctgtaca	aaagggaac	acatgtggac	taaaaaagat	gctgggaaaa	300
aagttgttcc	atgtagacat	gactggcatc	agactggagg	tgaagttacc	atttcagtat	360
atgctaaaaa	ctcacttcca	gaacttagcc	cgagtagaag	caaatagcac	attgtttaat	420
gtgcatattg	tatttgaagg	agagaaggaa	tttgatcaaa	atgtgaaatt	atgggggtgtg	480
attgatgtaa	agcgaattat	t				501

<210> 440
 <211> 481
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(481)
 <223> n = A,T,C or G

<400> 440						
tgatccctat	tgttttgtgg	agtttcatga	gcatcgtcat	gcagctgcag	cattagctgc	60
tatgaatgga	cggaagataa	tgggtaagga	agtcaaaagt	aattgggcaa	caacccttag	120
cagtcaaaaag	aaagatacaa	gcaatcattt	ccatgtcttt	gttgggtgatc	tcagcccaga	180
aattacaact	aaagatatata	aagctgcttt	tgaccatttt	ggaagaatat	cagatgcccg	240
agtggtaaaa	gacatggcaa	caggaaagtc	taagggatat	ggctttgtct	cctttttcaa	300
caaattgggat	gctgaaaacg	ccattcaaca	gatgggtggc	cagtggcttg	gtggaagaca	360
aatcagaact	aactgggcaa	cccgaagcc	tcccgctcca	aagagtacat	atgagtcaaa	420
taccaaacag	ctatcatatg	atganggtgt	aaatcagtct	aatccaagca	actgtctgta	480
t						481